

Rejections under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-3 and 23 under 35 U.S.C. § 103(a) as being unpatentable over either of Bateman *et al.* (*Gene Therapy*, 6, Suppl. 1:S6, Abstract 24, 1999) or Linardakis *et al.* (*Gene Therapy*, 6, Suppl. 1:S4, Abstract 13, 1999) for the reasons set forth in the office action mailed November 26, 2001. In response to Applicants' response filed May 28, 2002, the Examiner stated that:

Since whole attenuated measles virus compromises the membrane glycoproteins and causes cell death due to the formation of large multinucleated syncytial cells by the viral membrane fusogenic proteins, the teachings of Bateman point directly to the claimed method of reducing the number of viable cancer cells in a mammal by administration of an attenuated measles virus.

In addition, the Examiner stated that:

it is well known in the art that the cytotoxic effects caused by measles virus, which consist of the formation of non-viable large multinucleated syncytial cells, is affected through the FMGs on the surface of the virion. Even the name "fusogenic membrane glycoprotein" clearly points this out. Thus, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation that whole attenuated measles virus would have possessed the same fusogenic properties as those of the isolated FMGs. Applicant has provided no evidence to the contrary. Argument in the absence of evidence is not persuasive.

The Examiner also rejected claims 1-7, 9, 11-22, 24, and 28-33 under 35 U.S.C. § 103(a) as being unpatentable over Bateman *et al.* (*Cancer Research*, 60:1492-1497, 2000) in view of Weibel *et al.* (*Arch. Dis. Childhood*, 48:532-536, 1973) for the reasons set forth in the office action mailed November 26, 2001. In response to Applicants' response filed May 28, 2002, the Examiner stated that "one of ordinary skill in the art would have had a reasonable expectation of success for reducing tumor growth in a mammal by administration of an attenuated measles vaccine strain."

Lastly, the Examiner rejected (1) claims 1-7, 9, 11-22, 24, 26 and 28-33 under 35 U.S.C. § 103(a) as being unpatentable over Bateman *et al.* (*Cancer Research*, 60:1492-1497, 2000) in view of Usonis *et al.* (*Ped. Inf. Dis. J.*, 18:42-48, 1999), (2) claims 18 and 19 under 35 U.S.C. § 103(a) as being unpatentable over either of Bateman *et al.* (*Gene Therapy*, 6, Suppl. 1:S6, Abstract 24, 1999) in view of Weibel *et al.* (*Arch. Dis. Childhood*, 48:532-536, 1973) or

Bateman *et al.* (*Gene Therapy*, 6, Suppl. 1:S6, Abstract 24, 1999) in view of Usonis *et al.* (*Ped. Inf. Dis. J.*, 18:42-48, 1999) and further in view of Duprex *et al.* (*J. Virol.*, 73:9568-9575, 1999), and (3) claim 20 under 35 U.S.C. § 103(a) as being unpatentable over either of Galanis *et al.* (*Gene Therapy*, 6, Suppl. 1:S7, Abstract 28, 1999) or Russell *et al.* (*Proc. Am. Assoc. Cancer Res.*, 41:259, Abstract 1648, 2000) in view of either Weibel *et al.* (*Arch. Dis. Childhood*, 48:532-536, 1973) or Usonis *et al.* (*Ped. Inf. Dis. J.*, 18:42-48, 1999), for the reasons set forth in the office action mailed November 26, 2001.

Applicants respectfully disagree. Proper analysis under § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should carry out the claimed process, and (2) whether the prior art would also have revealed that in so carrying out, those of ordinary skill would have a reasonable expectation of success. *See, In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). It is axiomatic that in order to establish a *prima facie* case of obviousness under 35 U.S.C. § 103, a prior art reference must teach or suggest, alone or in combination with another prior art reference, each and every element of the claimed invention. *See, e.g.*, MPEP § 2143. The Federal Circuit warns that “both the suggestion and the expectation of success must be founded in the prior art, not in the applicant’s disclosure,” and that “it is impermissible to use the claimed invention as a ‘template’ to piece together the teachings of the prior art so that the claimed invention is rendered obvious.” *See, In re Dow Chemical Co.*, 837 F.2d 469 (Fed. Cir. 1988); *In re Fritch*, 972 F.2d 1260 (Fed Cir. 1992).

In addition, the so-called “secondary” considerations, such as unexpected results and long-felt but unmet need, should be considered in every case when present. *See, e.g., In re Sernaker*, 702 F.2d 989 (Fed. Cir. 1983) citing *In re Fielder and Underwood*, 471 F.2d 640 (Cust. & Pat. App. 1973). In fact, the Federal Circuit stated that:

evidence of secondary considerations may often be the most probative and cogent evidence in the record. It may often establish that an invention appearing to have been obvious in light of the prior art was not. It is to be considered as part of all the evidence, not just when the decisionmaker remains in doubt after reviewing the art.

Stratoflex, Inc., v. Aeroquip Corp., 713 F.2d 1530, 1538-39 (Fed. Cir. 1983).

Claim 1 recites a method for reducing the number of viable cancer cells in a mammal by administering attenuated measles virus to the mammal. Contrary to the Examiner's assertion, the Bateman *et al.* abstract does not "point directly" to the use of attenuated measles virus to reduce the number of viable cancer cells in a mammal. In fact, the Bateman *et al.* abstract never mentions administering an attenuated measles virus to a mammal to reduce the number of viable cancer cells in that mammal. Likewise, the combination of cited references does not suggest that those of ordinary skill in the art should administer an attenuated measles virus to a mammal to reduce the number of viable cancer cells in that mammal. In fact, at no point do the primary references (*i.e.*, the Bateman *et al.* abstract, the Bateman *et al.* publication, the Linardakis *et al.* abstract, the Galanis *et al.* abstract, or the Russell *et al.* abstract) discuss administering an attenuated measles virus, let alone administering an attenuated measles virus to a mammal to reduce the number of viable cancer cells in the mammal. The remaining secondary references do not cure the deficiencies of the primary references. The Duprex *et al.* reference merely discloses the use of a recombinant measles virus to monitor virus spread from cell to cell, while the Weibel *et al.* and Usonis *et al.* references merely disclose the use of attenuated measles viruses to vaccinate a child against measles. Thus, taken together, it is clear that a person having ordinary skill in the art at the time Applicants filed reading the cited references would not have been motivated to administer an attenuated measles virus to a mammal to reduce the number of viable cancer cells in that mammal.

Moreover, the combination of cited references fails to provide any information indicating that an attenuated measles virus can be administered to a mammal to reduce the number of viable cancer cells in the mammal. In fact, a person having ordinary skill in that art at the time Applicants filed, reading the cited references would not have had any information regarding the ability of an attenuated measles virus (*e.g.*, a nonpathogenic measles virus) to reduce the number of viable cancer cells in a mammal. Since the cited references fail to provide the required reasonable expectation of success in achieving reduction in the number of viable cancer cells in a mammal by administering an attenuated measles virus, the presently claimed invention is not obvious.

Even assuming for the sake of argument that the Examiner established a proper *prima facie* case of obviousness, the presently claimed invention is nevertheless not obvious as

evidenced by Applicants' surprising results supporting the claimed invention. At the time Applicants filed, a person having ordinary skill in that art would have understood that reducing the number of viable cancer cells in a mammal is generally an unpredictable process. Thus, Applicants' findings regarding attenuated measles viruses and cancer cell viability within a mammal are important and unexpected results. Specifically, Applicants' originally filed specification discloses the surprising findings that attenuated measles virus, when administered to a mammal, prevents tumor growth (*see, e.g.*, page 22), decreases the rate of tumor progression (*see, e.g.*, page 23 and Figures 2B and C), and causes tumor regression (*see, e.g.*, page 23 and Figure 2A). The unexpected nature of these findings highlights the non-obviousness of the presently claimed invention.

Additional evidence supporting the patentability of the presently claimed invention is the fact that the claimed invention satisfies a long-felt need that was recognized, persistent, and not solved by others. It is well established that the long-felt need is measured from the date the problem is identified, not the date of the most pertinent prior art references. *See, e.g.*, MPEP § 716.04 and *Texas Instruments Inc. v. Int'l Trade Comm'n*, 988 F.2d 1165, 1179 (Fed. Cir. 1993).

Having the ability to reduce the number of cancer cells within a mammal is a need that has existed for quite some time. For example, the Stenbeck *et al.* reference (*ACTA Oncologica*, 34:881-891 (1995)) discloses three decades of data relating to cancer survival. Thus, it is clear that cancer kills many people and effective cancer treatments are needed. This need has persisted through the years and continued to exist at the time of Applicants' invention as evidenced by the Cancer Statistics for 2000 published by the American Cancer Society. *See, Greenlee et al., CA Cancer J. Clin.*, 50:7-33 (2000). For the Examiner's convenience, copies of these two references are attached hereto.

Applicants' presently claimed invention fulfills this long-felt need. For example, claim 1 recites a method for reducing the number of viable cancer cells in a mammal by administering attenuated measles virus to the mammal. Applicants' specification provides multiple working examples demonstrating the effective treatment of cancer. In fact, Applicants' specification discloses the successful use of attenuated measles viruses to prevent tumor growth (*see, e.g.*, page 22), decrease the rate of tumor progression (*see, e.g.*, page 23 and Figures 2B and C), and cause tumor regression (*see, e.g.*, page 23 and Figure 2A). Thus, a person having ordinary skill

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in the art reading Applicants' specification would have understood that Applicants' invention provides an effective method for reducing the number of viable cancer cells in a mammal. This evidence supports the fact that the presently claimed invention is not obvious.

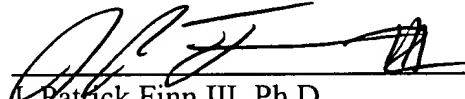
In light of the above, Applicants respectfully request that the rejection of claims 1-7, 9, 11-22, 24, 26, and 28-33 under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

Applicants submit that claims 1-7, 9, 11-22, 24, 26, and 28-33 are in condition for allowance, which action is requested. The Examiner is invited to call the undersigned agent at the telephone number below if such will advance prosecution of this application. Filed herewith is a check in payment of the Petition for Automatic Extension with the required fee. The Commissioner is authorized to charge any fees or credit any overpayments to Deposit Account No. 06-1050.

Respectfully submitted,

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Cancer Statistics, 2000

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Abstract

The Surveillance Research Program of the American Cancer Society's Department of Epidemiology and Surveillance Research reports its annual compilation of estimated cancer incidence, mortality, and survival data for the United States in the year 2000. After 70 years of increases, the recorded number of total cancer deaths among men in the US declined for the first time from 1996 to 1997. This decrease in overall male mortality is the result of recent downturns in lung and bronchus cancer deaths, prostate cancer deaths, and colon and rectum cancer deaths.

Despite decreasing numbers of deaths from female breast cancer and colon and rectum cancer, mortality associated with lung and bronchus cancer among women continues to increase. Lung cancer is expected to account for 25% of all female cancer deaths in 2000.

This report also includes a summary of global cancer mortality rates using data from the World Health Organization. (CA Cancer J Clin 2000;50:7-33.)

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This article is also available online at <http://www.ca-journal.org>.

Introduction

Cancer is an important public health concern in the United States and around the world. To provide an up-to-date perspective on the occurrence of cancer, the American Cancer Society presents an overview of cancer frequency, incidence, mortality, and survival statistics for the year 2000.

Methods

ESTIMATED NEW CANCER CASES

Because the US does not have a nationwide cancer registry, the exact number of new cases of cancer diagnosed each year in the US and in individual states is not known. Consequently, we first estimated the number of new cancer cases occurring annually in the US from 1979 through 1996 using population data reported by the US Bureau of the Census and age-specific cancer incidence rates collected by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program.¹ We fitted these annual cancer case estimates to an autoregressive quadratic model to forecast the number of cancer cases expected to be diagnosed in the US in the year 2000 (Table 1, Fig. 1).²

Between 1987 and 1992, the incidence rate of prostate cancer increased 85%, followed by a decline of 29% between 1992 and 1996.³ The sharp increase in incidence followed by the decline in recent years probably reflects extensive use of prostate-specific antigen (PSA) screening in a previously unscreened population and the subsequent increase in diagnoses at an early stage.⁴ We assumed that the number of prostate cancer cases would approximate the rates observed prior to widespread use of PSA screening, and there-

fore, we estimated new cases of prostate cancer for 2000 using a linear projection based on data from 1979 to 1989.

Because cancer incidence rates and case counts for 1979 through 1996 were not available for many states, we could not use the methods mentioned above to estimate new cases for individual states (Table 3). To derive these estimates, we assumed that the ratio of cancer deaths to cancer cases for each state was the same as the ratio for the US.²

ESTIMATED CANCER DEATHS

We estimated the number of cancer deaths expected to occur in the US in the year 2000 using underlying cause-of-death data from death certificates as reported to the National Center for Health Statistics (Table 2, Fig. 2).⁵ The recorded numbers of cancer deaths occurring annually from 1979 to 1997 were fitted to an autoregressive quadratic model to forecast the number of cancer deaths expected to occur in the US in 2000. The estimated number of cancer deaths for each state was calculated with the same modeling procedure used for the total US (Table 4).²

OTHER STATISTICS

Mortality statistics for the leading causes of death (Tables 6, 7, and 12), the leading causes of death from cancer (Tables 8, 9), and cancer mortality rates from 1930 to 1996 (Figs. 5, 6) were obtained using data from the National Center for Health Statistics.⁵ Incidence rates (Table 10, Figs. 3, 4), the probability of developing cancer (Table 5), and five-year relative survival rates (Tables 11, 13; Figs. 7, 8) were obtained from the SEER program.^{3,6} We computed global cancer mortality rates (Table 14) using data compiled by the World Health Organization.⁷ We included data from countries that have: 1) submitted data for at least one of the years between 1994 and 1997 using codes from the ninth or tenth revision of the International Classification of Diseases; 2) populations of 500,000 or more; 3) death

registration of at least 82%; and 4) a proportion of deaths with medically certified cause of death of at least 95%.⁸

Selected Findings

EXPECTED NUMBERS OF NEW CANCER CASES

In the year 2000, we estimate that about 1,220,100 new cases of invasive cancer will be diagnosed in the US (Table 1). This estimate does not include carcinoma in situ of any site except urinary bladder, and it does not include basal and squamous cell cancers of the skin. Approximately 1.3 million cases of basal and squamous cell skin cancers, 42,600 cases of breast carcinoma in situ, and 28,600 cases of in situ melanoma are expected to be newly diagnosed in 2000.

Among men, the most common cancers in 2000 are expected to be cancers of the prostate, lung and bronchus, and colon and rectum (Fig. 1). The prostate is the leading site for cancer incidence, accounting for 29% of new cancer cases in men. This year, 180,400 new cases of prostate cancer are expected to be diagnosed.

Among women, the three most commonly diagnosed cancers are expected to be cancers of the breast, lung and bronchus, and colon and rectum (Fig. 1). Cancers occurring at these sites are expected to account for over 50% of new cancer cases in women. Breast cancer alone is expected to account for 182,800 new cancer cases (30%) in 2000.

TRENDS IN CANCER INCIDENCE

For all sites combined, SEER cancer incidence rates appeared to peak in 1992 and decreased an average of -2.2% per year from 1992 to 1996.⁹ Similar declines have been seen recently for specific leading cancer sites (Figs. 3 and 4).

Breast cancer incidence rates have remained approximately level during the 1990s; however, they appear to be decreasing in younger women. Decreases in colon and rectum cancer incidence rates

began in the mid-1980s, and have been observed among both males and females in all racial/ethnic groups (with the exception of American Indian women in whom data were not sufficient to make a determination as to the direction of this trend).³ Incidence rates of colon and rectum cancer declined significantly between 1990 and 1996, on average -2.1% per year.⁹

A downturn in the incidence of lung and bronchus cancer in males began in the late 1980s, and between 1990 and 1996, incidence rates decreased significantly, -2.6% per year. Incidence rates of lung and bronchus cancer among females are stabilizing, and have begun to decline among women aged 40 to 59.⁹ Prostate cancer incidence rates also declined significantly between 1990 and 1996, on average -2.0% per year.

EXPECTED NUMBERS OF CANCER DEATHS

In 2000, an estimated 552,200 Americans are expected to die of cancer—more than 1,500 people a day (Table 2). Most cancer deaths in men (52%) in the year 2000 are expected to be from cancers of the lung and bronchus, prostate, and colon and rectum (Fig. 2).

Among women, cancers of the lung and bronchus, breast, and colon and rectum are expected to account for more than half of all cancer deaths in 2000 (Fig. 2). In 1987, lung cancer surpassed breast cancer as the leading cause of cancer death in women and is expected to account for 25% of all female cancer deaths in 2000.

TRENDS IN THE RECORDED NUMBER OF CANCER DEATHS

Following more than 70 years of increases, the recorded number of total cancer deaths among men in the US has declined for the first time, from a peak of 281,898 in 1996 to 281,110 in 1997. This promising change results from recent downturns in each of the top three causes of cancer death among men. Lung and bronchus cancer deaths among men declined from a peak of 92,493 in 1993 to 91,278 in 1997.

Prostate cancer deaths declined from a peak of 34,902 in 1994 to 32,891 in 1997. Colon and rectum cancer deaths among men were highest in 1990 at 28,635 and have declined to 28,075 in 1997.

Among women, the recorded number of total cancer deaths continues to increase, although the rate of increase has diminished in recent years. The upward trend among females is primarily due to sustained increases in the number of deaths from lung and bronchus cancer. The numbers of deaths from breast and colorectal cancers among females, however, have begun to decline. Breast cancer deaths were highest in 1995 at 43,844 and have declined to 41,943 in 1997. Colorectal cancer deaths among women have declined from a recent peak of 29,237 in 1995 to 28,621 in 1997, although these deaths reached their all-time high in 1984 at 29,522.

TRENDS IN CANCER DEATH RATES

Death rates for all cancers combined peaked in 1991 and decreased an average -0.7% per year from 1991 to 1996 (Figs. 5 and 6).⁹ Significant decreases have been seen among both males and females, persons younger than 65 years of age, and among whites, blacks, and Hispanics.

Breast cancer death rates in females decreased an average of -1.8% per year between 1990 and 1996; decreases were more pronounced among white women and among younger women. During the period from 1990 to 1996, colon and rectum cancer death rates decreased significantly, on average -1.7% per year.

Similar to trends in incidence, significant decreases in death rates for lung and bronchus cancer have occurred only among males (on average -1.6% per year between 1990 and 1996); rates among females recently have begun to slow and appear to be stabilizing. Prostate cancer death rates decreased on average -1.6% per year during the period between 1990 and 1996.

TRENDS IN CANCER BY RACE/ETHNICITY

Overall rates of cancer incidence vary considerably among racial and ethnic groups (Table 10). Blacks have the highest cancer incidence rates: They are about 60% more likely to develop cancer than are Hispanics and Asian/Pacific Islanders and more than twice as likely to develop cancer as American Indians. Between 1990 and 1996, incidence rates decreased among whites (-1.2% per year), Hispanics (-1.7% per year), and American Indians (-0.7% per year), and remained relatively stable among blacks and Asian/Pacific Islanders.³

White women are more likely to develop breast cancer than are women of other racial and ethnic groups, and black women are more likely to develop cancers of the colon and rectum.³ Black men have the highest incidence rates for cancers of the colon and rectum, lung and bronchus, and prostate. They are also at least 50% more likely to develop prostate cancer than men of other racial and ethnic groups.

Blacks are about 33% more likely to die of cancer than are whites, and more than twice as likely to die of cancer as are Asian/Pacific Islanders, American Indians, and Hispanics. Between 1990 and 1996, mortality rates decreased significantly among whites (-0.5% per year), blacks (-0.9% per year), and Hispanics (-0.6% per year); remained relatively stable among Asian/Pacific Islanders; and may be increasing among American Indians.³

Black women are more likely to die of breast (see article by Dignam in this issue of *CA*, page 50) and colon and rectum cancers than are women of any other racial or ethnic group, and they have approximately the same lung and bronchus cancer death rate as white women. As was seen with incidence rates, black men have the highest mortality rates of colon and rectum, lung and bronchus, and prostate cancers.³

CANCER IN CHILDREN


Cancer is the second leading cause of death among children between one and 14 years of age in the US; accidents are the most frequent cause of death in this age group (Table 12). The most commonly occurring cancers in children are leukemias (in particular, acute lymphocytic leukemia), tumors of the central and sympathetic nervous systems, lymphomas, soft-tissue sarcomas, and renal tumors.³ Over the past 20 years, there have been significant improvements in the five-year relative survival rate for many childhood cancers, especially acute lymphocytic and acute myeloid leukemia, non-Hodgkin's lymphoma, and Wilms' Tumor (Table 13). Between 1974/1976 and 1989/1995, five-year relative survival rates for childhood cancers at all sites combined improved from 56% to 75%.

Limitations and Future Challenges

Our estimates of the expected numbers of new cancer cases and cancer deaths should be interpreted with caution when tracking trends over time. These estimates may vary considerably from year to year, particularly for rare cancers and for states with smaller populations. We therefore discourage the use of these estimates to track year-to-year changes in cancer occurrence and death. The recorded number of cancer deaths and cancer death rates from the National Center for Health Statistics, and SEER cancer incidence rates are generally more informative statistics for the purpose of tracking cancer trends. For example, breast cancer incidence rates increased about 1% per year between 1979 and 1982, increased 4% per year between 1982 and 1987, and were approximately constant between 1987 and 1996. Despite the stabilization of incidence rates during the latter time period, the estimates of new breast cancer cases increased between 1988 and 1996.

Our estimates are based on the most currently available cancer mortality and

incidence data; however, these data are three and four years old, respectively, at the time that the estimates are calculated. As such, the effects of large changes occurring in the three- or four-year interval between 1996 or 1997 and 2000 cannot be captured by our modeling efforts. Finally, our estimates of new cancer cases are based on incidence rates for the geographic locations that participate in the SEER program and, therefore, may not be representative of the total US.

Despite these limitations, our estimates do describe current patterns of cancer incidence and mortality in the US. Such estimates will assist our continuing efforts to reduce the public health burden of cancer as we enter the 21st century. 

References

1. National Cancer Institute: SEER Cancer Incidence Public-Use Database, 1973-1996, August 1998 Submission. US Department of Health and Human Services, Public Health Service. Bethesda, MD, 1999.
2. Wingo PA, Landis S, Parker S, et al: Using cancer registry and vital statistics data to estimate the number of new cancer cases and deaths in the United States for the upcoming year. *J Reg Management* 1998;25:43-51.
3. Ries LAG, Kosary CL, Hankey BF, Miller BA, Edwards BK (eds). SEER Cancer Statistics Review, 1973-1996. National Cancer Institute, Bethesda, MD, 1997.
4. Wingo PA, Landis S, Ries LAG: An adjustment to the 1997 estimate for new prostate cancer cases. *CA Cancer J Clin* 1997;47:239-242.
5. National Center for Health Statistics, Division of Vital Statistics. Multiple Cause-of-Death for ICD9, 1996 Data Public-Use Documentation. (Web site) www.cdc.gov/nchswww/about/major/dvs/mcd/1996mcd.htm 1999.
6. DEVCAN: Probability of Developing or Dying of Cancer (Software), version 4. Feuer EJ, Wun LM. National Cancer Institute, Bethesda, MD, 1999.
7. World Health Organization: WHO Mortality Database. (Web site) www.who.int/whosis/mort 1999.
8. World Health Organization: World Health Statistics Annual, 1996. Geneva, Switzerland, 1997.
9. Wingo PA, Ries LAG, Giovino GA, et al. Annual report to the nation on the status of cancer 1973-1996, with a special section on lung cancer and tobacco smoking. *J Natl Cancer Inst* 1999;91: 675-690.

ANNOUNCING...

Continuing Medical Education in *CA—A Cancer Journal for Clinicians*

The American Cancer Society is pleased to announce that a Continuing Medical Education activity will be included in each upcoming issue of *CA—A Cancer Journal for Clinicians*.

When? Starting March/April 2000!

What? AMA PRA category 1 CME credits or AAFP Elective hours. *Topics to include management of cancer pain; malignant melanoma; new treatments for smoking cessation; lymphedema; and mind-body integration.*

How? Save each issue of *CA*. Review the article designated for CME credit. Complete the accompanying CME quiz and program evaluation. Submit by fax or mail for CME credit, according to instructions.

Who? The American Cancer Society, Inc., is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

Table 1
Estimated New Cancer Cases by Gender, US, 2000*

	Total	Male	Female
All Sites	1,220,100	619,700	600,400
Oral cavity & pharynx	30,200	20,200	10,000
Tongue	6,900	4,500	2,400
Mouth	10,900	6,500	4,400
Pharynx	8,200	5,900	2,300
Other oral cavity	4,200	3,300	900
Digestive system	226,600	117,600	109,000
Esophagus	12,300	9,200	3,100
Stomach	21,500	13,400	8,100
Small intestine	4,700	2,300	2,400
Colon	93,800	43,400	50,400
Rectum	36,400	20,200	16,200
Anus, anal canal, & anorectum	3,400	1,400	2,000
Liver & intrahepatic bile duct	15,300	10,000	5,300
Gallbladder & other biliary	6,900	2,900	4,000
Pancreas	28,300	13,700	14,600
Other digestive organs	4,000	1,100	2,900
Respiratory system	179,400	101,500	77,900
Larynx	10,100	8,100	2,000
Lung & bronchus	164,100	89,500	74,600
Other respiratory organs	5,200	3,900	1,300
Bones & joints	2,500	1,500	1,000
Soft tissue (including heart)	8,100	4,300	3,800
Skin (excluding basal & squamous)	56,900	34,100	22,800
Melanomas-skin	47,700	27,300	20,400
Other non-epithelial skin	9,200	6,800	2,400
Breast	184,200	17,400	182,800
Genital system	265,900	188,400	77,500
Uterine cervix	12,800		12,800
Uterine corpus	36,100		36,100
Ovary	23,100		23,100
Vulva	3,400		3,400
Vagina & other genital, female	2,100		2,100
Prostate	180,400	180,400	
Testis	6,900	6,900	
Penis & other genital, male	1,100	1,100	
Urinary system	86,700	58,600	28,100
Urinary bladder	53,200	38,300	14,900
Kidney & renal pelvis	31,200	18,800	12,400
Ureter & other urinary organs	2,300	1,500	800
Eye & orbit	2,200	1,200	1,000
Brain & other nervous system	16,500	9,500	7,000
Endocrine system	20,200	5,600	14,600
Thyroid	18,400	4,700	13,700
Other endocrine	1,800	900	900
Lymphoma	62,300	35,900	26,400
Hodgkin's disease	7,400	4,200	3,200
Non-Hodgkin's lymphoma	54,900	31,700	23,200
Multiple myeloma	13,600	7,300	6,300
Leukemia	30,800	16,900	13,900
Acute lymphocytic leukemia	3,200	1,800	1,400
Chronic lymphocytic leukemia	8,100	4,600	3,500
Acute myeloid leukemia	9,700	4,800	4,900
Chronic myeloid leukemia	4,400	2,600	1,800
Other leukemia	5,400	3,100	2,300
Other & unspecified primary sites	34,000	15,700	18,300

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

Table 2
Estimated Cancer Deaths by Gender, US, 2000*

	Total	Male	Female
All Sites	552,200	284,100	268,100
Oral cavity & pharynx	7,800	5,100	2,700
Tongue	1,700	1,100	600
Mouth	2,300	1,300	1,000
Pharynx	2,100	1,500	600
Other oral cavity	1,700	1,200	500
Digestive system	129,800	69,300	60,500
Esophagus	12,100	9,200	2,900
Stomach	13,000	7,600	5,400
Small intestine	1,200	600	600
Colon	47,700	23,100	24,600
Rectum	8,600	4,700	3,900
Anus, anal canal, & anorectum	500	200	300
Liver & intrahepatic bile duct	13,800	8,500	5,300
Gallbladder & other biliary	3,400	1,200	2,200
Pancreas	28,200	13,700	14,500
Other digestive organs	1,300	500	800
Respiratory system	161,900	93,100	68,800
Larynx	3,900	3,100	800
Lung & bronchus	156,900	89,300	67,600
Other respiratory organs	1,100	700	400
Bones & joints	1,400	800	600
Soft tissue (including heart)	4,600	2,200	2,400
Skin (excluding basal & squamous)	9,600	6,000	3,600
Melanomas-skin	7,700	4,800	2,900
Other non-epithelial skin	1,900	1,200	700
Breast	41,200	400	40,800
Genital system	59,000	32,500	26,500
Uterine cervix	4,600		4,600
Uterine corpus	6,500		6,500
Ovary	14,000		14,000
Vulva	800		800
Vagina & other genital, female	600		600
Prostate	31,900	31,900	
Testis	300	300	
Penis & other genital, male	300	300	
Urinary system	24,600	15,700	8,900
Urinary bladder	12,200	8,100	4,100
Kidney & renal pelvis	11,900	7,300	4,600
Ureter & other urinary organs	500	300	200
Eye & orbit	200	100	100
Brain & other nervous system	13,000	7,100	5,900
Endocrine system	2,100	1,000	1,100
Thyroid	1,200	500	700
Other endocrine	900	500	400
Lymphoma	27,500	14,400	13,100
Hodgkin's disease	1,400	700	700
Non-Hodgkin's lymphoma	26,100	13,700	12,400
Multiple myeloma	11,200	5,800	5,400
Leukemia	21,700	12,100	9,600
Acute lymphocytic leukemia	1,300	700	600
Chronic lymphocytic leukemia	4,800	2,800	2,000
Acute myeloid leukemia	7,100	3,900	3,200
Chronic myeloid leukemia	2,300	1,300	1,000
Other leukemia	6,200	3,400	2,800
Other & unspecified primary sites	36,600	18,500	18,100

*Excludes in situ carcinomas except urinary bladder.

Table 3
Estimated New Cancer Cases by Site and State, US, 2000*

State	All Sites	Female Breast	Uterine Cervix	Colon & Rectum	Uterine Corpus	Lung & Bronchus	Melanoma	Non-Hodgkin's Lymphoma	Kidney	Prostate	Urinary Bladder
Alabama	21,500	2,700	200	1,800	500	3,000	900	900	400	3,500	800
Alaska	1,500	200	—	200	—	200	100	100	—	100	100
Arizona	20,300	2,800	200	2,000	600	2,800	1,000	900	500	3,300	900
Arkansas	13,700	1,900	100	1,300	400	2,200	400	500	400	2,200	500
California	113,200	17,900	1,300	11,400	3,200	14,000	5,000	5,300	2,900	16,400	5,200
Colorado	13,400	2,000	100	1,400	400	1,500	700	700	400	1,800	600
Connecticut	15,400	2,300	100	1,500	500	1,900	600	700	400	2,300	800
Delaware	3,900	500	100	400	100	600	100	200	100	600	200
Dist. of Col.	2,700	500	—	300	100	300	—	100	—	600	100
Florida	88,100	12,000	900	9,100	2,500	12,600	3,500	4,000	2,000	13,700	4,300
Georgia	29,400	4,600	400	2,800	900	4,200	1,000	1,000	700	4,400	1,000
Hawaii	4,300	500	—	400	100	500	100	200	100	700	100
Idaho	4,700	700	—	500	100	600	200	200	200	800	200
Illinois	55,100	8,900	600	6,000	1,600	7,300	1,900	2,500	1,400	7,800	2,400
Indiana	27,900	4,200	300	3,100	800	4,000	1,000	1,200	800	3,900	1,200
Iowa	14,200	2,100	100	1,900	600	1,900	500	700	400	2,200	600
Kansas	11,900	1,600	100	1,200	300	1,600	500	500	300	1,800	500
Kentucky	20,500	2,700	300	2,200	500	3,400	900	800	600	2,600	600
Louisiana	20,800	3,200	300	2,200	500	2,900	700	800	600	3,200	700
Maine	6,800	900	100	700	100	1,000	200	300	200	900	400
Maryland	22,600	3,700	300	2,600	700	3,100	800	900	500	3,300	1,000
Massachusetts	30,100	4,400	200	3,500	800	3,900	1,300	1,400	700	4,200	1,700
Michigan	44,100	6,700	400	4,800	1,400	6,100	1,400	2,100	1,200	6,600	2,100
Minnesota	19,900	2,800	200	2,000	500	2,300	700	1,100	600	3,300	1,000
Mississippi	13,200	2,000	200	1,300	200	1,900	400	500	300	2,200	300
Missouri	27,000	3,700	300	2,900	800	4,000	1,100	1,100	700	3,600	1,100
Montana	4,100	600	—	400	100	500	100	200	100	700	200
Nebraska	7,300	1,100	100	1,000	200	900	200	300	200	1,000	300
Nevada	8,300	1,000	100	900	200	1,200	400	300	200	1,200	400
New Hampshire	5,500	700	—	600	100	700	200	300	100	700	300
New Jersey	40,000	6,400	400	4,600	1,500	4,800	1,700	1,900	1,000	5,600	2,100
New Mexico	6,600	1,000	100	700	200	700	300	300	200	1,200	200
New York	81,500	13,700	1,000	9,200	3,200	9,800	2,600	3,800	1,900	11,800	4,100
North Carolina	35,700	5,200	400	3,700	1,100	5,200	1,300	1,400	900	5,300	1,400
North Dakota	3,000	500	—	400	100	300	100	100	100	500	100
Ohio	56,100	8,600	600	6,200	2,000	7,800	1,900	2,700	1,500	7,800	2,500
Oklahoma	16,100	2,400	200	1,700	300	2,500	700	700	500	2,100	700
Oregon	15,800	2,200	100	1,600	400	2,200	700	700	400	2,700	700
Pennsylvania	66,600	10,500	600	7,800	2,200	8,600	2,400	3,000	1,700	10,000	3,100
Rhode Island	5,400	800	100	600	100	800	200	300	100	700	300
South Carolina	18,000	2,600	200	1,900	500	2,500	500	700	500	2,900	800
South Dakota	3,500	400	—	400	100	400	200	200	100	600	100
Tennessee	27,300	3,800	400	2,900	600	4,200	1,300	1,200	700	3,600	900
Texas	76,100	11,500	1,000	8,300	2,100	10,700	3,400	3,600	2,200	11,300	2,800
Utah	5,100	900	100	600	200	400	400	300	100	1,200	200
Vermont	2,700	400	100	400	100	400	200	100	100	300	100
Virginia	29,300	4,500	300	2,900	1,000	4,000	1,200	1,200	700	4,400	1,100
Washington	23,600	3,500	200	2,300	600	3,100	1,100	1,100	600	3,200	1,000
West Virginia	10,500	1,400	100	1,100	300	1,600	400	400	300	1,300	400
Wisconsin	23,600	3,300	200	2,500	700	2,800	1,000	1,200	700	3,800	1,200
Wyoming	2,000	300	—	300	100	200	100	100	100	400	—
United States†	1,220,100	182,800	12,800	130,200	36,100	164,100	47,700	54,900	31,200	180,400	53,200

— Estimate is 50 or fewer cases. State case estimates between 51 and 99 were rounded to 100.

* Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

† State estimates may not add up to United States total due to rounding.

Table 4
Estimated Cancer Mortality by Site and State, US, 2000*

State	Reported Death Rate per 100,000†	All Sites	Estimated Number of Deaths										
			Female Breast	Colon & Rectum	Liver	Leukemia	Lung & Bronchus	Non- Hodgkin's Lymphoma	Ovary	Pancreas	Prostate	Stomach	
Alabama	179	9,700	600	800	300	300	2,800	400	200	500	600	200	
Alaska	167	700	100	100	—	—	200	—	—	—	—	—	
Arizona	155	9,200	600	900	200	300	2,600	400	200	500	600	200	
Arkansas	181	6,200	400	600	200	200	2,100	300	200	300	400	100	
California	156	51,200	4,000	4,900	1,700	2,100	13,400	2,500	1,400	2,700	2,900	1,500	
Colorado	142	6,100	400	600	100	300	1,400	300	100	300	300	100	
Connecticut	163	7,000	500	600	200	300	1,900	300	200	400	400	200	
Delaware	195	1,800	100	200	—	100	500	100	—	100	100	—	
Dist. of Col.	212	1,200	100	100	—	—	300	—	—	100	100	100	
Florida	166	39,900	2,700	3,900	1,000	1,500	12,000	1,900	900	2,100	2,400	900	
Georgia	175	13,300	1,000	1,200	300	500	4,000	500	400	600	800	300	
Hawaii	133	2,000	100	200	100	100	500	100	—	100	100	100	
Idaho	148	2,100	200	200	—	100	500	100	100	100	100	—	
Illinois	178	24,900	2,000	2,600	700	1,000	6,900	1,200	700	1,300	1,400	600	
Indiana	178	12,600	900	1,300	300	500	3,900	600	300	600	700	200	
Iowa	160	6,400	500	800	100	300	1,800	300	200	300	400	100	
Kansas	159	5,400	400	500	100	200	1,600	200	100	300	300	100	
Kentucky	192	9,300	600	900	200	300	3,200	400	200	400	500	200	
Louisiana	193	9,400	700	1,000	300	400	2,700	400	200	500	600	300	
Maine	185	3,100	200	300	—	100	900	200	100	200	200	100	
Maryland	184	10,200	800	1,100	200	400	2,900	400	200	500	600	300	
Massachusetts	178	13,600	1,000	1,500	300	500	3,700	700	300	700	700	300	
Michigan	173	20,000	1,500	2,100	500	700	5,800	1,000	500	1,000	1,200	400	
Minnesota	156	9,000	600	900	200	400	2,200	500	200	500	600	200	
Mississippi	182	6,000	400	600	200	200	1,800	200	100	300	400	100	
Missouri	176	12,200	800	1,300	300	500	3,800	500	300	500	600	300	
Montana	159	1,900	100	200	100	100	500	100	100	100	100	—	
Nebraska	155	3,300	300	400	100	200	900	200	100	100	200	100	
Nevada	184	3,800	200	400	100	100	1,200	200	100	200	200	100	
New Hampshire	181	2,500	200	300	100	100	700	100	100	100	100	—	
New Jersey	179	18,100	1,400	2,000	500	800	4,600	900	500	1,000	1,000	500	
New Mexico	146	3,000	200	300	100	100	700	100	100	100	200	100	
New York	169	36,900	3,100	4,000	900	1,400	9,400	1,800	1,000	2,200	2,100	1,100	
North Carolina	175	16,200	1,200	1,600	300	600	5,000	700	400	800	900	300	
North Dakota	155	1,300	100	200	—	100	300	100	—	100	100	—	
Ohio	180	25,400	1,900	2,700	500	1,000	7,400	1,300	600	1,300	1,400	500	
Oklahoma	170	7,300	500	700	200	300	2,400	300	200	300	400	100	
Oregon	166	7,100	500	700	100	300	2,100	300	200	400	500	100	
Pennsylvania	177	30,100	2,300	3,400	700	1,200	8,200	1,400	800	1,500	1,800	600	
Rhode Island	178	2,400	200	300	100	100	800	100	100	100	100	100	
South Carolina	178	8,200	600	800	200	300	2,400	300	200	400	500	200	
South Dakota	155	1,600	100	200	—	100	400	100	—	100	100	—	
Tennessee	181	12,400	900	1,200	300	400	4,000	600	300	600	600	300	
Texas	168	34,400	2,600	3,600	1,100	1,400	10,300	1,700	900	1,700	2,000	900	
Utah	122	2,300	200	200	100	100	400	100	100	100	200	40	
Vermont	172	1,200	100	200	—	—	400	100	—	—	100	—	
Virginia	177	13,300	1,000	1,300	300	500	3,800	600	300	600	800	300	
Washington	162	10,700	800	1,000	300	500	3,000	500	300	500	600	200	
West Virginia	184	4,800	300	500	100	200	1,500	200	100	200	200	100	
Wisconsin	163	10,700	700	1,100	200	500	2,700	600	300	600	700	200	
Wyoming	157	900	100	100	—	—	200	—	—	—	100	—	
United States‡	170	552,200	40,800	56,300	13,800	21,700	156,900	26,100	14,000	28,200	31,900	13,000	

— Estimate is 50 or fewer deaths. State death estimates between 51 and 99 were rounded to 100.

* Excludes in situ carcinomas except urinary bladder.

† Average annual mortality rate between 1992 and 1996, age-adjusted to the 1970 US standard population.

Source: US Mortality 1992-1996, National Center for Health Statistics, Centers for Disease Control and Prevention 1999, Surveillance, Epidemiology, and End Results Program, Division of Cancer Control and Population Sciences, National Cancer Institute.³

‡ State estimates may not add up to United States total due to rounding.

Figure 1
Estimated New Cancer Cases*
10 Leading Sites by Gender, US, 2000

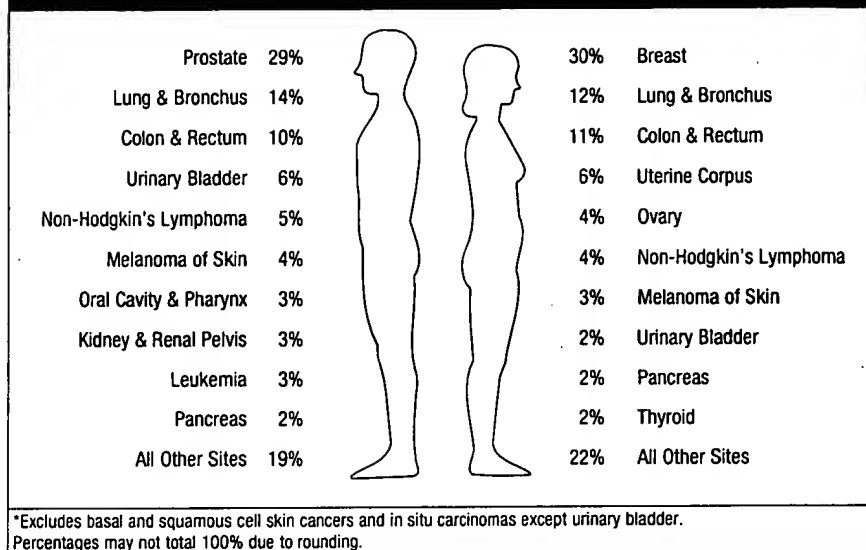


Figure 2
Estimated Cancer Deaths*
10 Leading Sites by Gender, US, 2000

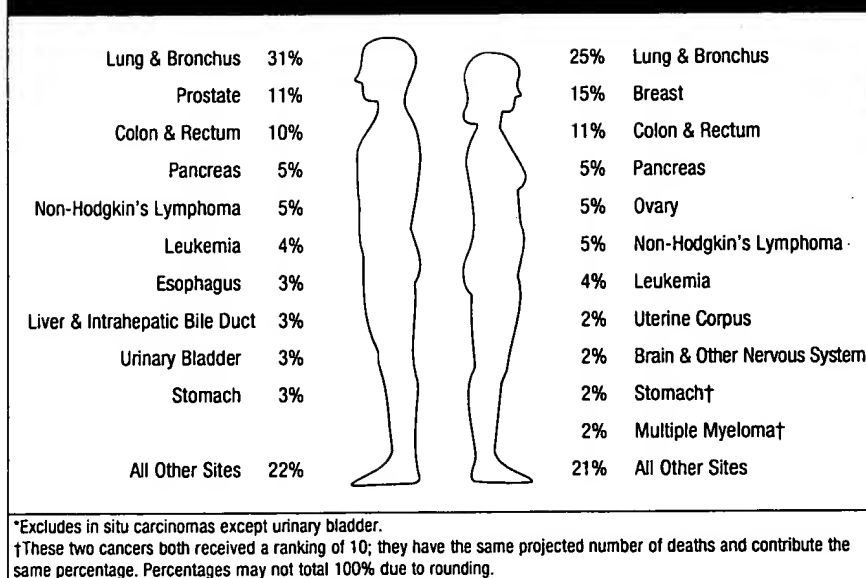


Table 5
Probability of Developing Invasive Cancers Over Selected Age Intervals,
by Gender, US, 1994-1996*

		Birth to 39 (%)	40 to 59 (%)	60 to 79 (%)	Birth to Death (%)
All sites†	Male	1.61 (1 in 62)	8.17 (1 in 12)	33.65 (1 in 3)	43.56 (1 in 2)
	Female	1.94 (1 in 52)	9.23 (1 in 11)	22.27 (1 in 4)	38.11 (1 in 3)
Breast	Female	0.43 (1 in 235)	4.06 (1 in 25)	6.88 (1 in 15)	12.56 (1 in 8)
	Male	0.06 (1 in 1,579)	0.85 (1 in 124)	3.97 (1 in 29)	5.64 (1 in 18)
Colon & Rectum	Female	0.05 (1 in 1,947)	0.67 (1 in 149)	3.06 (1 in 33)	5.55 (1 in 18)
	Male	0.04 (1 in 2,592)	1.29 (1 in 78)	6.35 (1 in 16)	8.11 (1 in 12)
Lung & Bronchus	Female	0.03 (1 in 2,994)	0.94 (1 in 106)	3.98 (1 in 25)	5.69 (1 in 18)
	Male	(Less than 1 in 10,000)	1.90 (1 in 53)	13.69 (1 in 7)	15.91 (1 in 6)

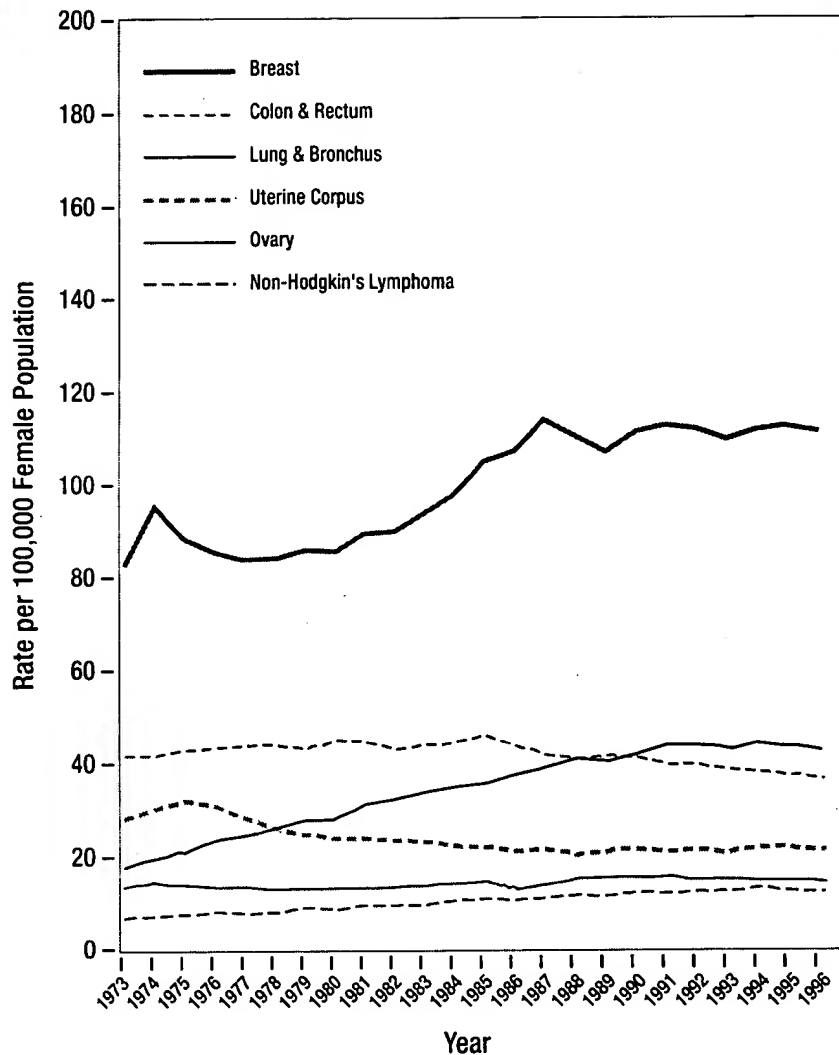
*Of those free of cancer at beginning of age interval and based on cancer cases diagnosed between 1994 and 1996.

The "1 in" statistic and the inverse of the percentage may not be equivalent due to rounding.

†Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

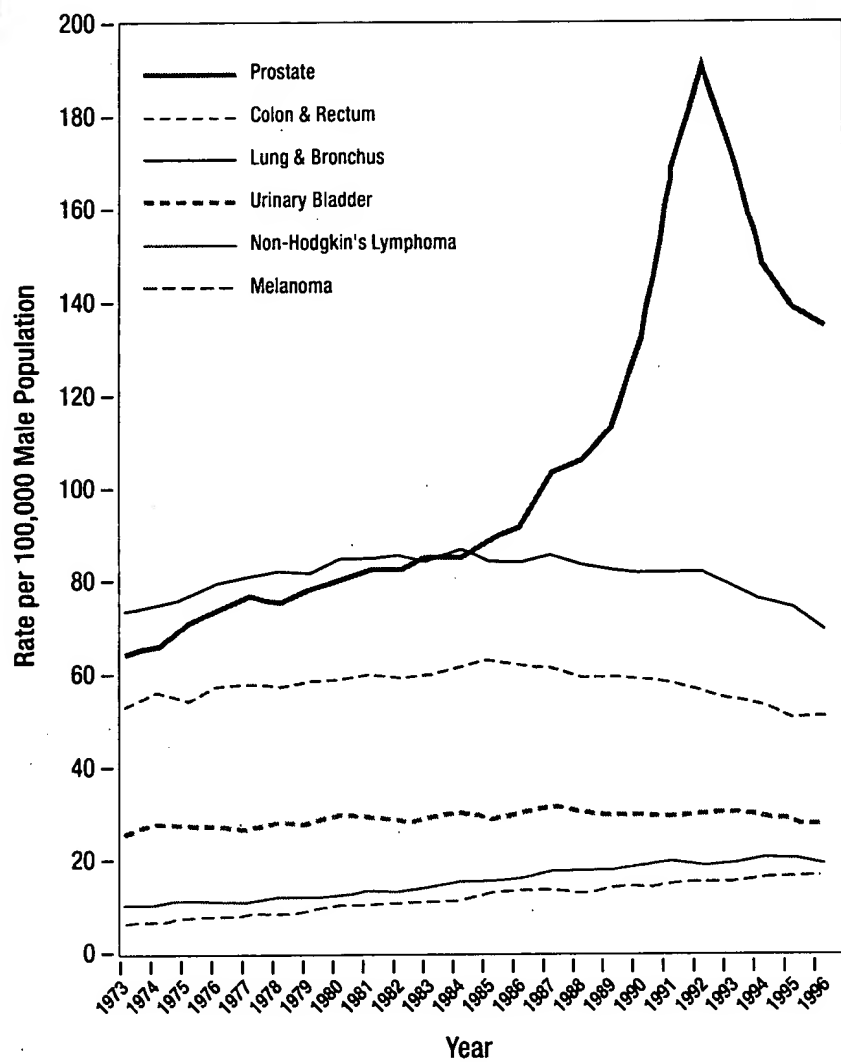
Source: Surveillance, Epidemiology, and End Results Program, 1973-1996, Division of Cancer Control and Population Sciences, National Cancer Institute, DEVCAN Software, Version 4.0, National Cancer Institute.⁶

Figure 3
Age-Adjusted Cancer Incidence Rates*
for Females by Site, US, 1973-1996



* Rates are per 100,000 population and are age-adjusted to the 1970 US standard population.
 Source: Surveillance, Epidemiology, and End Results Program, 1973-1996, Division of Cancer Control and Population Sciences, National Cancer Institute.³

Figure 4
Age-Adjusted Cancer Incidence Rates*
for Males by Site, US, 1973-1996



* Rates are per 100,000 population and are age-adjusted to the 1970 US standard population.
 Source: Surveillance, Epidemiology, and End Results Program, 1973-1996, Division of Cancer Control and Population Sciences, National Cancer Institute.³

Table 6
Reported Deaths for the 10 Leading Causes of Death
by Age and Gender, US, 1997

	All Ages		Ages 1-19		Ages 20-39	
	Male	Female	Male	Female	Male	Female
1.	All Causes 1,154,039	All Causes 1,160,206	All Causes 18,149	All Causes 9,685	All Causes 69,832	All Causes 31,150
	Heart Diseases 356,598	Heart Diseases 370,376	Accidents 7,882	Accidents 4,097	Accidents 20,240	Accidents 6,463
2.	Cancer 281,110	Cancer 258,467	Homicide 2,740	Cancer 963	Suicide 9,426	Cancer 6,159
3.	Cerebro- vascular Diseases 62,564	Cerebro- vascular Diseases 97,227	Suicide 1,723	Homicide 710	Homicide 8,669	Heart Diseases 2,794
4.	Accidents 61,963	Chronic Obstructive Pulmonary Diseases 53,045	Cancer 1,207	Congenital Anomalies 570	HIV Infection 5,994	Suicide 2,037
5.	Chronic Obstructive Pulmonary Diseases 55,984	Pneumonia & Influenza 47,165	Congenital Anomalies 683	Suicide 386	Heart Diseases 5,833	Homicide 2,001
6.	Pneumonia & Influenza 39,284	Diabetes Mellitus 34,449	Heart Diseases 557	Heart Diseases 385	Cancer 5,467	HIV Infection 1,918
7.	Diabetes Mellitus 28,187	Accidents 33,681	Cerebral Palsy 241	Pneumonia & Influenza 200	Cirrhosis of Liver 1,149	Cerebro- vascular Diseases 878
8.	Suicide 24,492	Alzheimer's Disease 15,437	Pneumonia & Influenza 215	Cerebral Palsy 186	Cerebro- vascular Diseases 878	Diabetes Mellitus 619
9.	Cirrhosis of Liver 16,260	Nephritis 13,191	Chronic Obstructive Pulmonary Diseases 165	Benign Neoplasms 103	Diabetes Mellitus 842	Cirrhosis of Liver 571
10.	Homicide 15,449	Septicemia 12,741	Peripheral Nervous System Diseases 148	Chronic Obstructive Pulmonary Diseases 101	Pneumonia & Influenza 730	Pneumonia & Influenza 505

Source: US Mortality Public Use Data Tape 1997, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Table 6 (Continued)

Ages 40-59		Ages 60-79		Ages 80+	
Male	Female	Male	Female	Male	Female
All Causes 182,834	All Causes 111,414	All Causes 513,377	All Causes 410,559	All Causes 353,742	All Causes 585,057
Heart Diseases 51,356	Cancer 45,781	Heart Diseases 168,426	Cancer 131,274	Heart Diseases 130,028	Heart Diseases 231,179
Cancer 47,118	Heart Diseases 19,744	Cancer 161,581	Heart Diseases 115,982	Cancer 65,685	Cancer 74,240
Accidents 15,507	Accidents 5,779	Chronic Obstructive Pulmonary Diseases 31,528	Cerebro- vascular Diseases 27,798	Cerebro- vascular Diseases 28,609	Cerebro- vascular Diseases 63,175
Cirrhosis of Liver 7,642	Cerebro- vascular Diseases 5,175	Cerebro- vascular Diseases 26,491	Chronic Obstructive Pulmonary Diseases 27,501	Pneumonia & Influenza 21,773	Pneumonia & Influenza 34,046
Suicide 7,568	Diabetes Mellitus 4,032	Diabetes Mellitus 15,082	Diabetes Mellitus 16,310	Chronic Obstructive Pulmonary Diseases 20,368	Chronic Obstructive Pulmonary Diseases 21,682
Cerebro- vascular Diseases 6,295	Chronic Obstructive Pulmonary Diseases 3,372	Pneumonia & Influenza 13,576	Pneumonia & Influenza 10,443	Diabetes Mellitus 7,302	Diabetes Mellitus 13,453
HIV Infection 6,109	Cirrhosis of Liver 2,814	Accidents 10,650	Accidents 7,145	Accidents 7,163	Alzheimer's Disease 12,215
Diabetes Mellitus 4,921	Suicide 2,405	Diseases of Arteries 8,289	Diseases of Arteries 5,300	Nephritis 5,599	Accidents 9,853
Chronic Obstructive Pulmonary Diseases 3,478	Pneumonia & Influenza 1,805	Cirrhosis of Liver 6,461	Nephritis 4,624	Diseases of Arteries 5,044	Atherosclerosis 8,017
Homicide 2,963	HIV Infection 1,446	Nephritis 5,136	Cirrhosis of Liver 4,269	Alzheimer's Disease 4,663	Nephritis 7,530

Source: US Mortality Public Use Data Tape 1997, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Table 7
Fifteen Leading Causes of Death, US, 1997

Rank	Cause of Death	Number of Deaths	Death Rate per 100,000 Population*	Percent (%) of Total Deaths†
	All Causes	2,314,245	654.3	100.0
1	Heart Diseases	726,974	194.6	31.4
2	Cancer	539,577	164.1	23.3
3	Cerebrovascular Diseases	159,791	40.8	6.9
4	Chronic Obstructive Pulmonary Diseases	109,029	30.6	4.7
5	Accidents	95,644	31.5	4.1
6	Pneumonia & Influenza	86,449	21.2	3.7
7	Diabetes Mellitus	62,636	18.3	2.7
8	Suicide	30,535	10.2	1.3
9	Diseases of Arteries	27,792	7.7	1.2
10	Nephritis	25,331	6.7	1.1
11	Cirrhosis of Liver	25,175	8.2	1.1
12	Alzheimer's Disease	22,475	5.2	1.0
13	Septicemia	22,396	6.1	1.0
14	Homicide	19,846	7.3	0.9
15	HIV Infection	16,516	5.0	0.7
	Other & Ill-defined	344,079		14.9

*Age-adjusted to the 1970 US standard population.
†Percentages may not total 100% due to rounding.
Source: US Mortality Public Use Data Tape 1997, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Table 8
Reported Deaths for the Five Leading Cancer Sites
for Males by Age, US, 1997

All Ages	< 20	20-39	40-59	60-79	≥80
All Sites 281,110	All Sites 1,252	All Sites 5,467	All Sites 47,118	All Sites 161,581	All Sites 65,685
Lung & Bronchus 91,278	Leukemia 423	Non-Hodgkin's Lymphoma 723	Lung & Bronchus 15,379	Lung & Bronchus 59,558	Lung & Bronchus 15,823
Prostate 32,891	Brain & ONS 288	Leukemia 662	Colon & Rectum 4,347	Prostate 16,277	Prostate 15,511
Colon & Rectum 28,075	Endocrine System 115	Brain & ONS 625	Pancreas 2,584	Colon & Rectum 15,842	Colon & Rectum 7,459
Pancreas 13,470	Bones & Joints 86	Lung & Bronchus 512	Non-Hodgkin's Lymphoma 2,552	Pancreas 7,898	Urinary Bladder 2,900
Non-Hodgkin's Lymphoma 12,286	Non-Hodgkin's Lymphoma 86	Colon & Rectum 412	Esophagus 2,069	Non-Hodgkin's Lymphoma 6,383	Pancreas 2,843

Note: "All Sites" excludes in situ carcinomas except urinary bladder.

ONS = other nervous system.

Source: US Mortality Public Use Data Tape 1997, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Table 9
Reported Deaths for the Five Leading Cancer Sites
for Females by Age, US, 1997

All Ages	< 20	20-39	40-59	60-79	≥80
All Sites 258,467	All Sites 1,009	All Sites 6,159	All Sites 45,781	All Sites 131,274	All Sites 74,240
Lung & Bronchus 61,922	Leukemia 322	Breast 1,629	Breast 12,093	Lung & Bronchus 38,488	Lung & Bronchus 12,879
Breast 41,943	Brain & ONS 253	Uterine Cervix 629	Lung & Bronchus 10,088	Breast 18,385	Colon & Rectum 12,046
Colon & Rectum 28,621	Soft Tissue 85	Lung & Bronchus 462	Colon & Rectum 3,426	Colon & Rectum 12,799	Breast 9,835
Pancreas 14,205	Endocrine System 79	Leukemia 462	Ovary 2,801	Pancreas 7,437	Pancreas 5,045
Ovary 13,507	Bones & Joints 71	Brain & ONS 385	Uterine Cervix 1,803	Ovary 7,207	Non-Hodgkin's Lymphoma 3,859

Note: "All Sites" excludes in situ carcinomas except urinary bladder.

ONS = other nervous system.

Source: US Mortality Public Use Data Tape 1997, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Table 10
Incidence and Mortality Rates* by Site, Race,
and Ethnicity, US, 1990-1996

Site	White	Black	Asian/Pacific Islander	American Indian	Hispanic†
INCIDENCE					
All Sites					
Total	402.9	442.9	279.1	153.4	275.4
Male	480.2	598.0	325.5	177.8	326.9
Female	351.6	335.6	244.9	136.8	243.2
Breast (Female)	113.2	99.3	72.6	33.9	69.4
Colon & Rectum					
Total	43.9	50.4	38.6	16.4	29.0
Male	53.2	58.1	47.5	21.5	35.7
Female	36.8	44.9	31.4	12.4	24.0
Lung & Bronchus					
Total	55.9	73.9	35.8	18.6	27.6
Male	73.1	112.3	52.4	25.3	38.8
Female	43.3	46.2	22.5	13.5	19.6
Prostate	147.3	222.9	81.5	46.5	102.8
MORTALITY					
All Sites					
Total	167.5	223.4	103.4	104.0	104.9
Male	208.8	308.8	129.2	123.3	131.8
Female	139.8	168.1	83.5	90.2	86.3
Breast (Female)	25.7	31.4	11.4	12.3	15.3
Colon & Rectum					
Total	17.4	23.1	10.9	9.9	10.4
Male	21.5	27.8	13.4	11.0	13.2
Female	14.5	20.0	9.0	8.9	8.4
Lung & Bronchus					
Total	49.3	60.5	23.7	28.8	19.9
Male	70.1	100.8	34.9	40.5	32.0
Female	33.8	32.8	14.9	19.8	11.0
Prostate	23.7	54.8	10.7	14.3	16.7

Note: Incidence data are from the 11 SEER areas; mortality data are from all states except Connecticut, Oklahoma, Louisiana, and New Hampshire.

*Rates are per 100,000 population and are age-adjusted to the 1970 US standard population.

†Hispanic is not mutually exclusive of white, black, Asian/Pacific Islander, or American Indian.

Sources: Surveillance, Epidemiology, and End Results Program 1973-1996, Division of Cancer Control and Population Sciences, National Cancer Institute² (Incidence); US Mortality 1973-1996, National Center for Health Statistics, Centers for Disease Control and Prevention 1999, Surveillance, Epidemiology, and End Results Program, Division of Cancer Control and Population Sciences, National Cancer Institute³ (Mortality).

Table 11
Trends in Five-Year Relative Cancer Survival Rates* (%)
by Race and Year of Diagnosis, US, 1974-1995

	1974- 1976	1980- 1982	1989- 1995	1974- 1976	1980- 1982	1989- 1995	1974- 1976	1980- 1982	1989- 1995
Site	White			Black			All Races		
All Sites	51	52	61†	39	40	48†	50	51	59†
Brain	22	25	30†	27	31	39†	22	25	30†
Breast (Female)	75	77	86†	63	66	71†	75	76	85†
Colon	51	56	62†	46	49	52†	50	55	62†
Esophagus	5	7	13†	4	5	9†	5	7	12†
Hodgkin's Disease	72	75	83†	69	72	76	71	75	82†
Kidney	52	51	61†	49	55	58†	52	52	60†
Larynx	66	69	66	60	58	53	66	68	65
Leukemia	35	39	44†	31	33	34	34	39	43†
Liver	4	4	6†	2	2	3	4	4	5†
Lung & Bronchus	13	14	14†	12	12	11	13	13	14†
Melanoma of Skin	80	83	88†	67†	61§	68†	80	83	88†
Multiple Myeloma	24	28	28†	28	29	31	24	28	28†
Non-Hodgkin's Lymphoma	48	52	52†	48	50	41†	47	51	51†
Oral Cavity & Pharynx	55	55	56	36	31	34	53	53	53
Ovary	37	39	50†	41	39	47†	37	39	50†
Pancreas	3	3	4†	3	5	4†	3	3	4†
Prostate	68	75	93†	58	65	84†	67	73	92†
Rectum	49	53	60†	42	38	51†	49	52	60†
Stomach	15	17	19†	17	19	22	15	18	21†
Testis	79	92	96†	76†	90†	88	79	92	95†
Thyroid	92	94	95†	88	94	89	92	94	95†
Urinary bladder	74	79	82†	48	58	62†	73	78	81†
Uterine Cervix	70	68	71†	64	61	59	69	67	70
Uterine Corpus	89	83	86†	61	54	56	88	82	84†

*Survival rates are adjusted for normal life expectancy and are based on follow-up of patients through 1996.

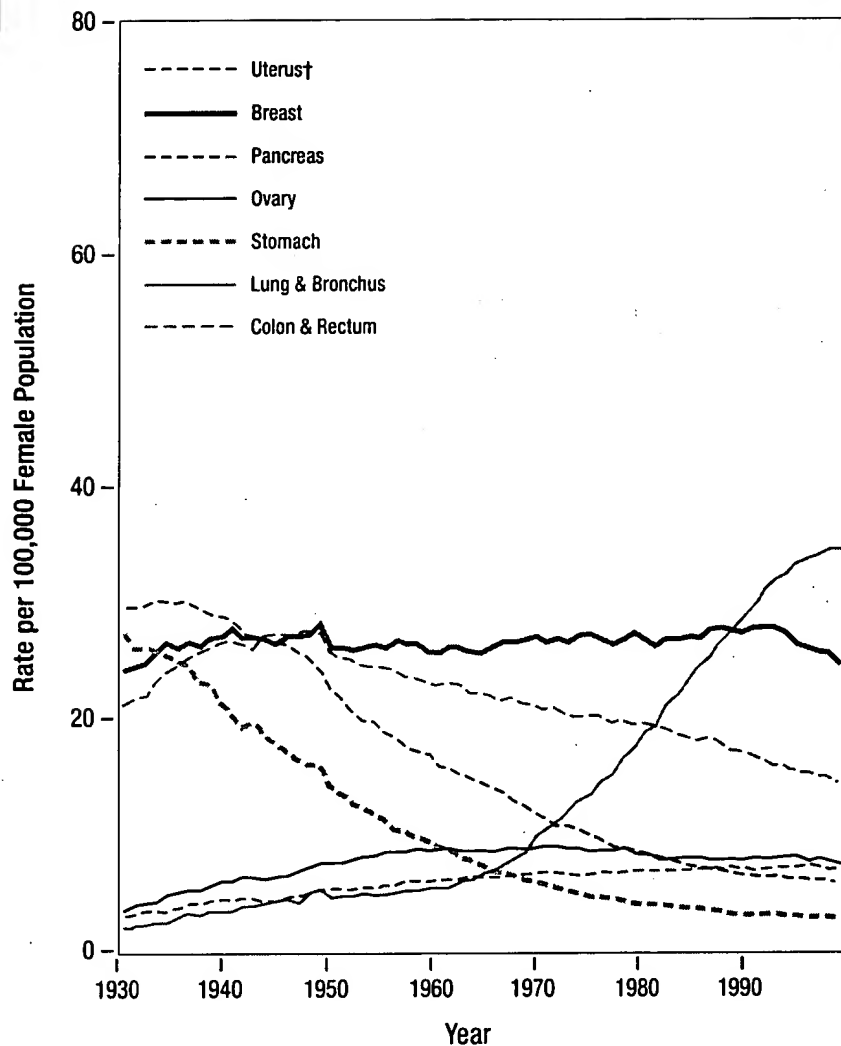
†The difference in rates between 1974-1976 and 1989-1995 is statistically significant ($p < 0.05$).

‡The standard error of the survival rate is between five and 10 percentage points.

§The standard error of the survival rate is greater than 10 percentage points.

Source: Surveillance, Epidemiology and End Results Program 1973-1996, Division of Cancer Control and Population Sciences, National Cancer Institute.³

Figure 5
Age-Adjusted Cancer Death Rates* for Females by Site,
US, 1930-1996



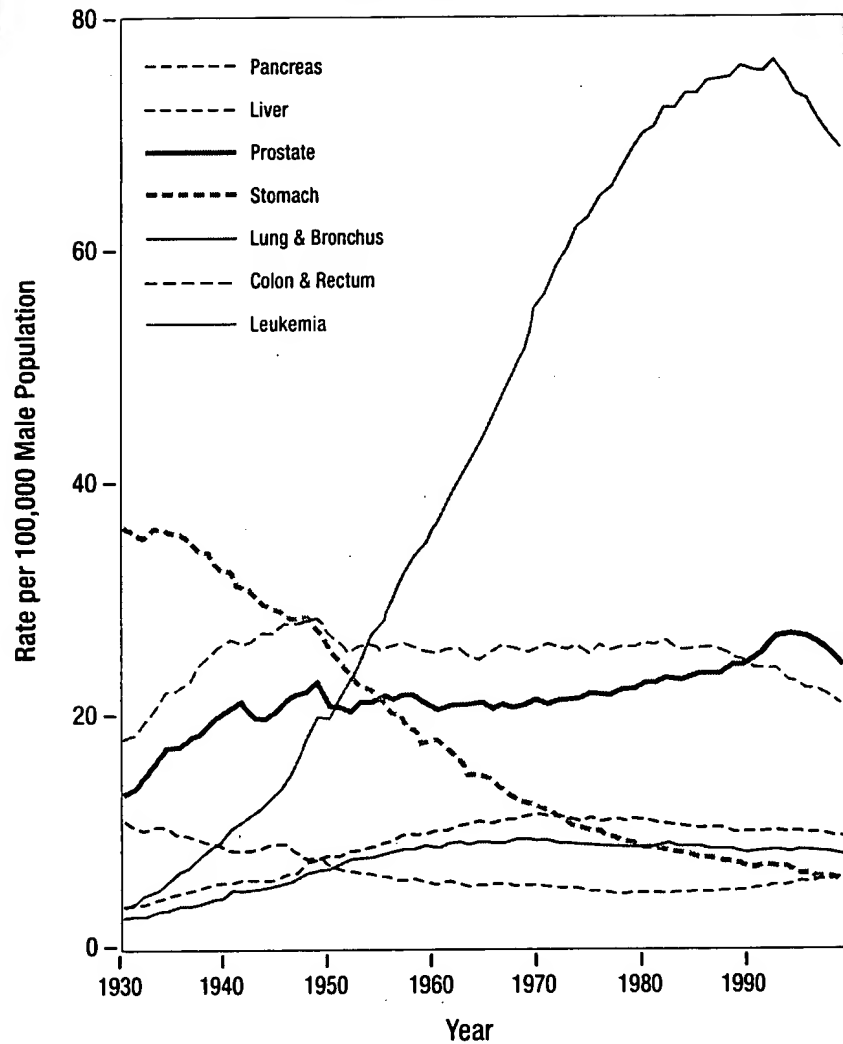
Note: Due to changes in the ICD coding, numerator information has changed over time. Rates for cancer of the uterus, ovary, lung & bronchus, and colon & rectum are affected by these coding changes.

* Rates are per 100,000 population and are age-adjusted to the 1970 US standard population.

† Uterine cancer death rates are for uterine cervix and uterine corpus combined.

Source: US Mortality Public Use Data Tapes 1960-1996, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Figure 6
Age-Adjusted Cancer Death Rates* for Males by Site,
US, 1930-1996

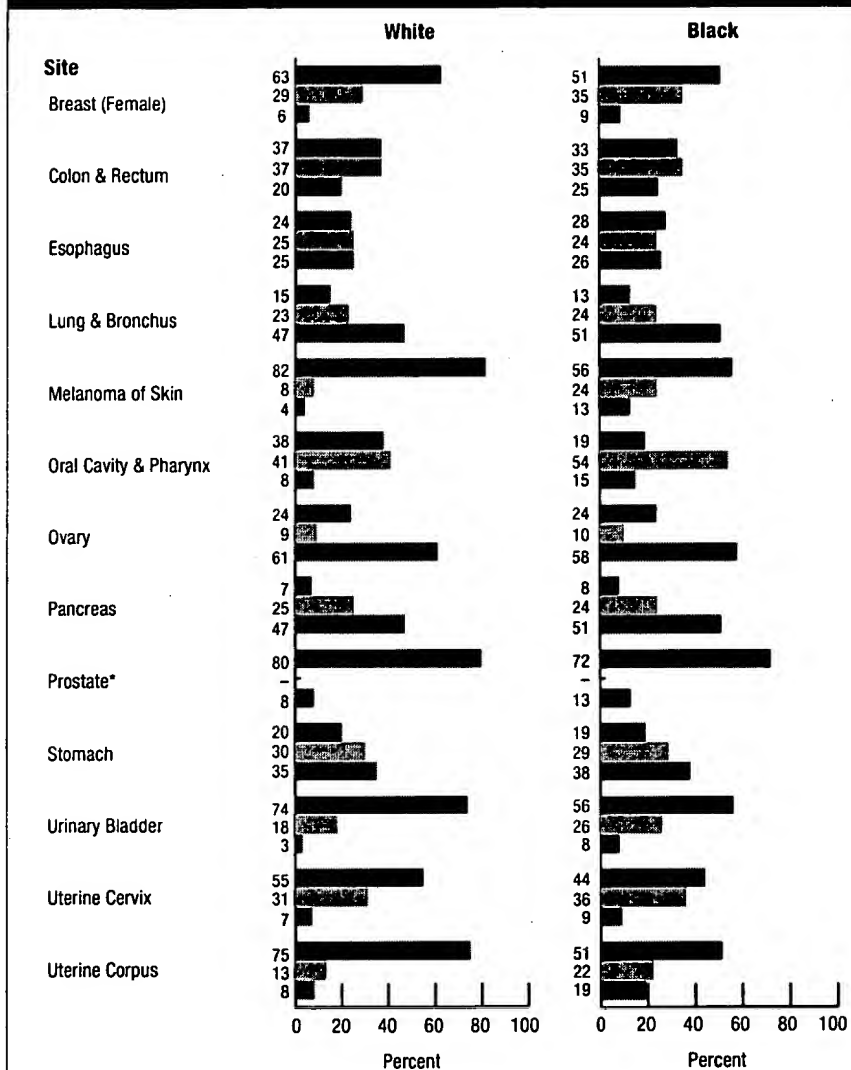


Note: Due to changes in the ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung & bronchus, and colon & rectum are affected by these coding changes.

* Rates are per 100,000 population and are age-adjusted to the 1970 US standard population.

Source: US Mortality Public Use Data Tapes 1960-1996, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Figure 7
Percent Distribution of Cancer Cases by Race and Stage at Diagnosis, US, 1989-1995



*The rate for local stage represents local and regional stages combined.

Note: Staging according to SEER summary stage categories rather than the American Joint Committee on Cancer (AJCC) staging system. For each site and race, stage categories do not total 100% because sufficient information is not available to assign a stage to all cancer cases.

Source: Surveillance, Epidemiology, and End Results Program 1973-1996, Division of Cancer Control and Population Sciences, National Cancer Institute.³




Localized 
 Regional 
 Distant 

Figure 8
Five-Year Relative Survival Rates by Race and
Stage at Diagnosis, US, 1989-1995

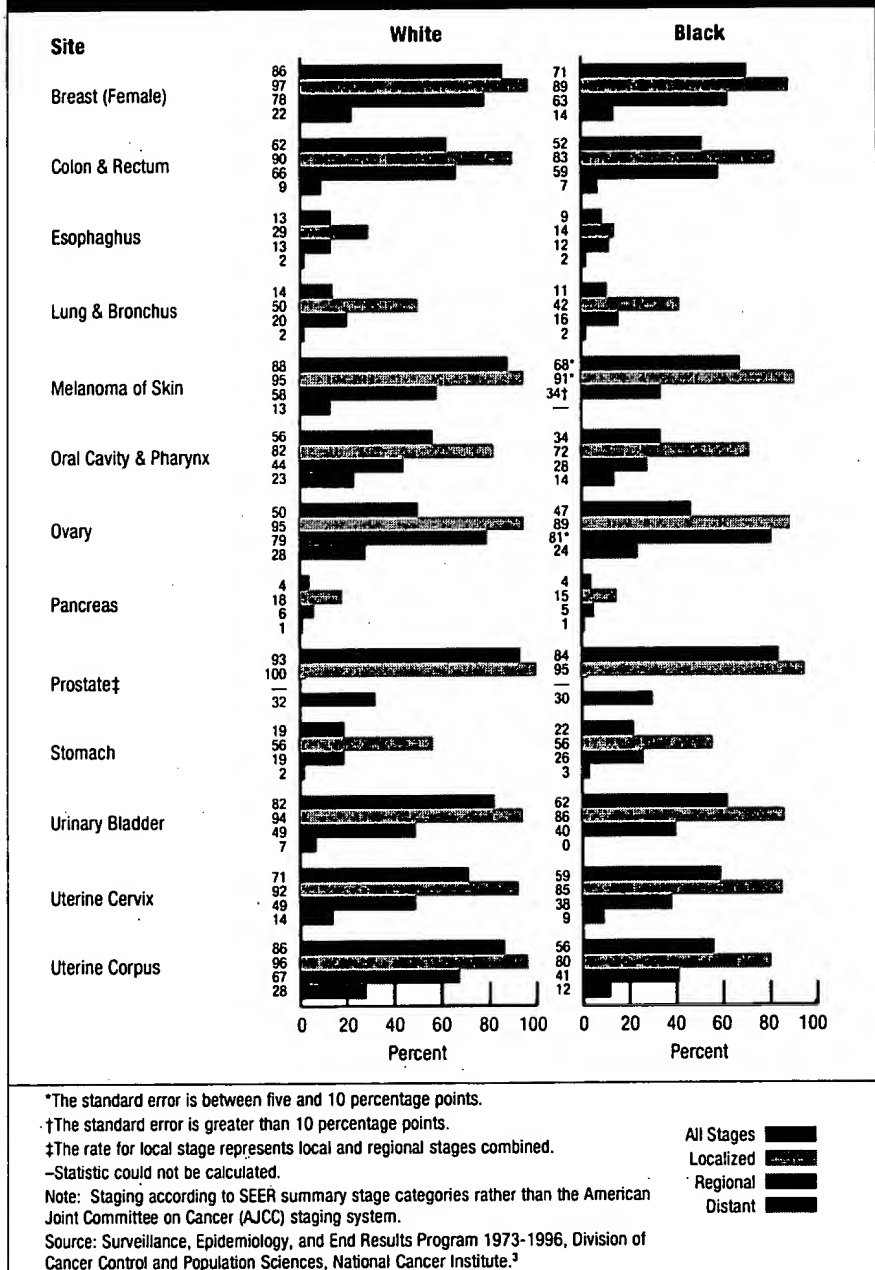


Table 12
Fifteen Leading Causes of Death Among Children
Aged 1-14 Years, US, 1997

Rank	Cause of Death	Number of Deaths	Death Rate per 100,000 Population*	Percent (%) of Total Deaths†
	All Causes	13,562	24.6	100.0
1	Accidents	5,376	9.8	39.6
2	Cancer	1,468	2.7	10.8
3	Congenital Anomalies	1,036	1.8	7.6
4	Homicide	832	1.5	6.1
5	Heart Diseases	525	1.0	3.9
6	Pneumonia & Influenza	321	0.6	2.4
7	Cerebral Palsy	313	0.6	2.3
8	Suicide	307	0.6	2.3
9	Chronic Obstructive Pulmonary Diseases	170	0.3	1.3
10	HIV Infection	156	0.3	1.2
11	Benign Neoplasms	141	0.3	1.0
12	Cerebrovascular Diseases	132	0.2	1.0
13	Septicemia	125	0.2	0.9
14	Viral Diseases	107	0.2	0.8
15	Anemias	103	0.2	0.8
	All Others	2,450		18.1

* Age-adjusted to the 1970 US standard population.

† Percentages may not total 100% due to rounding.

Source: US Mortality Public Use Data Tape 1997, National Center for Health Statistics, Centers for Disease Control and Prevention, 1999.

Table 13
Trends in Five-Year Relative Cancer Survival Rates* (%)
for Children Under Age 15, US, 1974-1995

Site	Five-Year Relative Survival Rates (%)					
	Year of Diagnosis					
	1974-1976	1977-1979	1980-1982	1983-1985	1986-1988	1989-1995
All Sites	56	62	65	68	70	75†
Acute Lymphocytic Leukemia	53	67	71	69	78	81†
Acute Myeloid Leukemia	14	28†	21†	32†	32†	43†
Bones and Joints	53†	53†	54†	57†	62†	67†
Brain & Other Nervous System	55	56	55	62	62	64†
Hodgkin's Disease	78	84	91	90	90	93†
Neuroblastoma	53	54	53	55	59	71†
Non-Hodgkin's Lymphoma	44	51	61	71	70	77†
Soft Tissue	61	69	65	76	66	77†
Wilms' Tumor	74	78	87	86	91	93†

Note: "All sites" excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

* Survival rates are adjusted for normal life expectancy and are based on follow-up of patients through 1996.

† The difference in rates between 1974-1976 and 1989-1995 is statistically significant ($p < 0.05$).

‡ The standard error of the survival rate is between five and 10 percentage points.

Source: Surveillance, Epidemiology, and End Results Program 1973-1996, Division of Cancer Control and Population Sciences, National Cancer Institute.³

Table 14
Cancer Around the World: Age-Adjusted Death Rates* per 100,000 Population
for Selected Sites for 45 Countries, 1994-1997

Country	All Sites		Oral		Colon & Rectum		Breast		Prostate		Lung		Uterus		Stomach		Leukemia	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
United States†	156.0 (24)	108.3 (7)	3.2 (29)	1.1 (23)	15.2 (27)	10.4 (23)	20.0 (14)	15.9 (20)	52.3 (13)	26.6 (2)	2.4 (34)	2.5 (33)	4.4 (44)	2.0 (44)	6.3 (5)	3.7 (10)	6.3 (5)	3.7 (10)
Australia‡	156.7 (22)	98.2 (25)	4.1 (26)	1.2 (12)	20.2 (10)	13.3 (10)	19.9 (15)	19.0 (9)	38.8 (29)	13.6 (10)	2.6 (31)	1.7 (43)	6.6 (40)	2.7 (43)	6.1 (6)	3.6 (11)	6.1 (6)	3.6 (11)
Austria‡	161.0 (21)	99.9 (22)	6.0 (18)	1.1 (27)	21.7 (8)	12.2 (14)	20.9 (13)	16.9 (14)	40.7 (26)	10.3 (16)	2.6 (33)	4.0 (20)	12.8 (24)	6.9 (24)	4.8 (24)	3.2 (18)	4.8 (24)	3.2 (18)
Azerbaijan§	117.0 (40)	62.8 (45)	2.3 (38)	0.4 (45)	6.0 (41)	4.2 (43)	8.6 (42)	5.1 (41)	22.3 (38)	3.7 (45)	1.8 (39)	3.7 (23)	24.9 (10)	9.5 (15)	3.9 (38)	2.7 (38)	3.9 (38)	2.7 (38)
Bulgaria¶	150.0 (28)	86.5 (32)	4.9 (21)	0.8 (39)	17.2 (20)	11.4 (19)	15.9 (31)	8.5 (34)	43.7 (23)	6.6 (32)	4.9 (18)	5.7 (5)	18.5 (19)	8.8 (17)	4.9 (23)	3.0 (33)	4.9 (23)	3.0 (33)
Canada‡	156.2 (23)	105.6 (13)	3.8 (27)	1.2 (17)	16.1 (26)	10.3 (25)	21.5 (10)	16.4 (17)	50.0 (14)	23.0 (3)	1.9 (35)	2.2 (38)	6.2 (42)	3.0 (41)	5.5 (17)	3.2 (22)	5.5 (17)	3.2 (22)
Chile¶	142.5 (32)	105.3 (14)	2.1 (42)	0.6 (43)	7.0 (38)	6.7 (36)	12.1 (35)	16.0 (19)	20.5 (39)	6.4 (33)	10.6 (3)	2.8 (31)	32.2 (3)	11.7 (8)	4.2 (34)	2.7 (39)	4.2 (34)	2.7 (39)
China**	149.9 (29)	83.5 (37)	2.6 (36)	1.1 (24)	7.9 (36)	6.4 (37)	5.0 (44)	-	37.3 (30)	15.8 (8)	3.0 (27)	-	26.9 (6)	12.7 (4)	3.7 (40)	3.0 (31)	3.7 (40)	3.0 (31)
Colombia¶	97.7 (43)	88.1 (29)	2.1 (41)	1.2 (19)	4.8 (44)	5.1 (40)	9.1 (40)	12.6 (28)	14.3 (44)	6.8 (30)	9.9 (5)	4.5 (16)	21.4 (13)	13.1 (3)	4.3 (33)	3.7 (9)	4.3 (33)	3.7 (9)
Croatia#	212.0 (6)	98.7 (24)	11.4 (4)	1.0 (29)	22.5 (6)	11.5 (18)	18.5 (20)	13.0 (25)	65.1 (6)	8.9 (20)	2.9 (29)	4.9 (9)	20.9 (14)	8.5 (19)	5.7 (12)	3.1 (25)	5.7 (12)	3.1 (25)
Cuba‡	127.2 (35)	91.8 (27)	5.5 (20)	1.5 (4)	9.4 (34)	11.3 (20)	14.9 (33)	20.8 (4)	35.7 (31)	12.6 (12)	5.3 (15)	8.3 (1)	6.4 (41)	3.2 (38)	4.6 (28)	3.3 (17)	4.6 (28)	3.3 (17)
Czech Republic§	229.3 (3)	124.7 (3)	7.0 (13)	1.2 (16)	34.3 (1)	17.3 (3)	21.1 (12)	16.0 (18)	67.9 (4)	11.4 (14)	5.0 (17)	5.2 (8)	15.5 (23)	7.3 (22)	7.0 (2)	4.2 (6)	7.0 (2)	4.2 (6)
Denmark§	178.6 (14)	140.0 (1)	4.5 (23)	1.6 (3)	22.7 (5)	15.6 (4)	27.6 (1)	19.9 (6)	49.1 (16)	28.0 (1)	3.8 (21)	3.5 (24)	6.6 (38)	3.1 (40)	6.0 (10)	3.9 (7)	6.0 (10)	3.9 (7)
Estonia§	206.2 (8)	102.8 (20)	9.5 (7)	1.3 (7)	18.1 (16)	12.2 (13)	18.5 (19)	12.8 (27)	66.4 (5)	7.0 (28)	5.7 (13)	4.6 (14)	26.0 (8)	12.0 (6)	6.8 (3)	4.9 (1)	6.8 (3)	4.9 (1)
Finland‡	142.3 (33)	85.0 (34)	2.2 (39)	1.0 (33)	12.1 (31)	8.5 (31)	16.8 (25)	17.6 (12)	41.2 (25)	6.9 (29)	1.0 (43)	2.4 (34)	10.2 (30)	4.7 (32)	4.7 (25)	3.2 (21)	4.7 (25)	3.2 (21)
France‡	188.2 (12)	84.8 (35)	11.3 (5)	1.3 (9)	16.6 (22)	9.6 (29)	19.6 (16)	15.8 (21)	46.5 (19)	6.1 (34)	1.6 (42)	3.4 (26)	7.2 (37)	2.8 (42)	5.6 (14)	3.3 (16)	5.6 (14)	3.3 (16)
Germany†	169.5 (17)	103.3 (17)	6.5 (15)	1.2 (14)	20.8 (9)	14.0 (9)	21.7 (8)	16.6 (16)	45.4 (20)	9.4 (17)	2.8 (30)	2.8 (30)	12.0 (26)	6.3 (27)	5.5 (16)	3.5 (14)	5.5 (16)	3.5 (14)
Greece§	145.7 (31)	78.2 (41)	1.9 (44)	0.6 (44)	8.0 (35)	6.2 (38)	16.2 (27)	9.3 (33)	49.8 (15)	7.1 (25)	0.9 (44)	2.3 (35)	8.2 (36)	4.3 (34)	6.0 (9)	3.6 (12)	6.0 (9)	3.6 (12)
Hungary**	272.2 (1)	138.4 (2)	20.0 (1)	2.4 (1)	34.3 (2)	18.7 (2)	23.7 (6)	18.7 (11)	85.6 (1)	20.3 (5)	6.5 (10)	4.8 (13)	18.8 (18)	8.7 (18)	7.4 (1)	4.4 (4)	7.4 (1)	4.4 (4)
Ireland‡	171.6 (16)	121.0 (5)	4.4 (24)	1.3 (8)	22.5 (7)	13.3 (9)	26.1 (2)	18.8 (10)	44.5 (22)	18.6 (7)	3.1 (26)	2.3 (36)	10.7 (28)	5.1 (30)	4.6 (27)	3.0 (34)	4.6 (27)	3.0 (34)
Israel§	127.1 (36)	104.5 (15)	1.5 (45)	0.7 (40)	17.9 (18)	13.8 (8)	25.1 (4)	12.0 (30)	27.1 (35)	8.7 (21)	1.7 (41)	3.0 (27)	8.6 (34)	5.1 (31)	6.1 (8)	4.2 (5)	6.1 (8)	4.2 (5)
Japan#	155.2 (25)	75.7 (42)	3.1 (31)	0.8 (37)	17.1 (21)	9.9 (28)	7.7 (43)	5.1 (42)	31.7 (33)	8.5 (22)	1.9 (36)	2.0 (42)	30.2 (4)	12.3 (5)	4.1 (36)	2.5 (41)	4.1 (36)	2.5 (41)

Kazakhstan†	207.6 (7)	102.9 (19)	7.7 (11)	1.9 (2)	12.6 (30)	8.6 (30)	13.2 (34)	5.7 (39)	62.3 (10)	8.5 (23)	6.2 (12)	4.8 (15)	33.1 (2)	13.9 (2)	3.3 (43)	2.6 (40)
Kyrgyzstan†	123.5 (37)	72.4 (43)	3.6 (28)	1.0 (31)	6.9 (39)	4.5 (41)	10.6 (37)	4.3 (43)	25.5 (36)	4.3 (40)	6.2 (11)	3.5 (25)	29.1 (5)	10.7 (10)	2.5 (45)	2.0 (45)
Latvia†	224.0 (4)	107.6 (9)	7.9 (10)	1.2 (21)	18.3 (12)	11.8 (15)	17.3 (24)	11.5 (31)	63.6 (8)	5.9 (37)	4.2 (19)	5.4 (7)	26.8 (7)	11.8 (7)	5.8 (11)	3.8 (8)
Lithuania†	203.7 (10)	101.0 (21)	8.5 (9)	1.0 (30)	18.2 (13)	11.7 (16)	18.7 (18)	15.2 (22)	62.5 (9)	5.3 (38)	7.4 (7)	4.8 (12)	25.9 (9)	10.2 (11)	6.6 (4)	4.5 (3)
Macedonia†	137.4 (34)	82.3 (38)	2.6 (35)	0.7 (42)	10.8 (33)	7.1 (34)	16.1 (30)	6.2 (38)	39.6 (28)	6.7 (31)	3.1 (25)	5.5 (6)	22.0 (11)	9.7 (13)	4.4 (31)	2.4 (42)
Meuritus†	80.3 (45)	65.2 (44)	4.3 (25)	1.2 (20)	6.0 (42)	3.8 (44)	9.0 (41)	7.7 (36)	16.7 (42)	4.0 (41)	5.5 (14)	8.3 (2)	10.8 (27)	5.7 (28)	3.5 (41)	2.1 (44)
Mexico†	85.0 (44)	78.9 (40)	1.9 (43)	0.7 (41)	3.6 (45)	3.3 (45)	9.3 (39)	12.8 (26)	16.2 (43)	6.0 (35)	14.0 (1)	2.1 (41)	9.7 (31)	7.1 (23)	3.9 (39)	3.1 (28)
Netherlands†	182.3 (13)	108.0 (8)	2.8 (33)	1.0 (32)	17.7 (19)	12.7 (11)	26.0 (3)	19.4 (8)	62.0 (11)	13.6 (9)	1.7 (40)	2.2 (37)	10.3 (29)	4.2 (35)	5.7 (13)	3.1 (29)
New Zealand†	167.2 (18)	121.2 (4)	2.7 (34)	1.2 (13)	26.4 (3)	19.1 (1)	22.9 (7)	19.8 (7)	39.6 (27)	18.8 (6)	3.4 (23)	2.1 (40)	6.0 (43)	3.2 (39)	6.1 (7)	4.5 (2)
Norway†	146.6 (30)	103.3 (18)	3.1 (30)	1.0 (34)	20.0 (11)	14.7 (5)	19.4 (17)	23.2 (2)	31.7 (32)	13.3 (11)	3.1 (24)	2.9 (29)	9.1 (33)	4.6 (33)	4.3 (32)	2.8 (37)
Poland†	204.9 (9)	107.6 (11)	6.3 (17)	1.1 (25)	16.4 (23)	11.0 (22)	16.1 (29)	11.1 (32)	71.3 (2)	11.1 (15)	7.3 (8)	3.8 (22)	18.9 (17)	6.8 (25)	5.6 (15)	3.5 (15)
Portugal†	155.0 (26)	84.3 (36)	6.4 (16)	0.8 (38)	18.1 (15)	10.4 (24)	17.6 (22)	17.2 (13)	29.2 (34)	4.6 (39)	2.6 (32)	4.1 (18)	21.8 (12)	10.0 (12)	5.0 (22)	3.2 (19)
Rep. of Moldova†	162.4 (20)	88.9 (30)	11.7 (3)	1.3 (10)	16.2 (25)	11.1 (21)	18.2 (21)	5.7 (40)	43.0 (24)	6.0 (36)	6.6 (9)	4.4 (17)	20.7 (15)	9.2 (16)	5.2 (20)	3.1 (26)
Romania†	150.7 (27)	88.5 (31)	7.1 (12)	1.2 (18)	11.3 (32)	7.9 (33)	15.7 (32)	8.3 (35)	44.8 (21)	7.2 (24)	10.5 (4)	4.1 (19)	17.6 (21)	6.8 (26)	4.5 (29)	3.0 (30)
Russian Fed†	237.1 (2)	107.6 (10)	9.1 (8)	1.1 (26)	18.2 (14)	12.6 (12)	16.1 (28)	7.2 (37)	70.5 (3)	7.0 (27)	5.0 (16)	4.9 (11)	36.9 (1)	15.3 (1)	5.1 (21)	3.5 (13)
Slovakia†	218.1 (5)	103.5 (16)	16.8 (2)	1.2 (15)	14.6 (28)	6.8 (35)	-	-	12.2 (29)	64.2 (7)	7.1 (28)	-	-	-	3.4 (42)	2.2 (43)
Slovenia†	200.9 (11)	107.4 (12)	10.7 (6)	1.0 (28)	23.9 (4)	14.0 (6)	21.2 (11)	14.7 (23)	61.1 (12)	9.1 (19)	4.0 (20)	4.9 (10)	19.7 (16)	8.3 (20)	5.4 (18)	3.2 (20)
Spain†	173.2 (15)	79.8 (39)	7.0 (14)	0.9 (36)	16.4 (24)	10.0 (27)	17.5 (23)	13.9 (24)	48.7 (17)	3.9 (42)	1.8 (38)	3.0 (28)	12.7 (25)	5.6 (29)	5.2 (19)	3.2 (23)
Sweden†	123.3 (38)	94.4 (26)	2.2 (40)	0.9 (35)	13.8 (29)	10.2 (26)	16.8 (26)	21.4 (3)	22.3 (37)	12.0 (13)	1.8 (37)	2.5 (32)	6.6 (39)	3.5 (37)	4.5 (30)	3.2 (24)
Trinidad & Tobago†	107.3 (41)	99.4 (23)	4.6 (22)	1.4 (6)	7.8 (37)	8.3 (32)	21.5 (9)	35.5 (1)	11.2 (45)	3.7 (44)	8.2 (6)	7.1 (4)	8.4 (35)	7.7 (21)	4.2 (35)	2.9 (36)
Turkmenistan†	120.8 (39)	86.0 (33)	5.8 (19)	1.5 (5)	6.2 (40)	4.4 (42)	9.5 (38)	1.4 (44)	17.3 (41)	3.7 (43)	3.7 (22)	3.8 (21)	18.3 (20)	11.0 (9)	3.1 (44)	2.9 (35)
United Kingdom†	164.2 (19)	116.5 (6)	2.9 (32)	1.1 (22)	18.0 (17)	11.6 (17)	24.5 (5)	16.6 (15)	46.6 (18)	20.5 (4)	3.0 (28)	2.1 (39)	9.5 (32)	3.9 (36)	4.7 (26)	3.0 (32)
Venezuela†	104.3 (42)	90.0 (28)	2.5 (37)	1.2 (11)	5.9 (43)	6.2 (39)	11.8 (36)	20.3 (5)	19.4 (40)	9.3 (18)	10.8 (2)	7.4 (3)	16.8 (22)	9.7 (14)	4.1 (37)	3.1 (27)

Note: Figures in parentheses represent order of rank within site and sex group.

* Rates are age-adjusted to the World Health Organization world standard population.

† 1994-1997; ‡ 1994-1995; § 1994-1996; ¶ 1994 only; ** 1996-1997; # 1995-1996; ## 1995-1997.

& Oral cancer mortality rate includes nasopharynx only.

- Data not available

Source: Mortality Database 1994-1997, World Health Organization, 1999.

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CANCER SURVIVAL IN SWEDEN DURING THREE DECADES, 1961-1991

MAGNUS STENBECK, MÅNS ROSÉN and LARS-ERIK HOLM

Cancer survival in Sweden in 1961-1991 is presented as a comprehensive report from the Swedish Cancer Registry. The report shows both successes and failures, confirms some earlier published results and presents some new findings worth further analysis. Survival has increased for female breast cancer, malignant melanoma, cancers of the testis and thyroid gland, acute leukemia, and Hodgkin's disease. No improvements are found for multiple myeloma or cancers of the liver, gall bladder, and pancreas. Small increases are shown for colorectal cancer and cancers of the stomach, oesophagus, and kidney. Increases in postoperative survival are shown for sites dominated by histologically benign tumors, i.e., intracranial neurinoma, meningioma, and cancers of the endocrine glands such as parathyroid tumors. From 1970-1972 to 1980-1982 the 10-year relative survival rate (RSR) increased from 30% to 38% for males and from 44% to 51% for females. Hence, cancer survival for all cases combined has approached the survival of the general population somewhat. Most of the increases took place in the 1970's. Changes in the distribution of incidence towards cancer sites with better prognoses account for some 10-20% of the observed increases in RSR, whereas the aging of the cancer population reduces the upward trend in RSR for all cases combined by some 1-2%. Cancer patients have poorer survival than the population long after 5 years of follow-up. They reach the survival of the population after about 8-12 years for colorectal cancer, 10 years for cervical cancer, 7-10 years for malignant melanoma, 13-18 years for kidney cancer, and more than 19 years for female breast and prostate cancer. For patients diagnosed in 1970-1972 this occurred 16 years after diagnosis at 29% for males and 43% for females when all cancer cases were combined. The extended time until 'statistical cure' for most cancer forms clearly indicates the need to augment the commonly used 5-year RSR with other outcome measures. If cancers on average are discovered earlier today, the 5-year RSR gives an exaggerated impression of the improvement over time. In this case the change in the 10-year RSR is a less biased criterion.

Several studies on cancer survival in Sweden have been published for specific cancer sites (1-7) and for all cancers combined (8). However, in a supplement to *Acta Oncologica* vol. 34, 1995, the first comprehensive survival analysis of cancer patients in Sweden is presented for the three

decades during which a national cancer registry has been kept (9). Such comprehensive reports have also been presented from the other Nordic countries (10-13).

Comprehensive and national cancer survival reports constitute reference materials for clinicians, oncologists and scientists involved in clinical work, medical auditing, or research. They provide a basis for evaluation decision-making, and for the debate concerning the effects of cancer treatment and prevention, and they act as overall sources of information on the survival of groups of patients diagnosed with cancer.

In addition, the present report can be used to discuss how the concepts of survival and cure should be defined

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and measured. Two problems are the limitations of short follow-up periods and the usefulness of the concept of "statistical cure". These issues were critically discussed more than 40 years ago (14-15), but many scientific articles still use 1, 2 and 5-year relative survival as their main outcome measure.

Sometimes there are good reasons for the use of short follow-up periods. They are appropriate for evaluating postoperative mortality and survival trends for very malignant cancers when the survival pattern of the population is reached early for a small group of patients due to high mortality in the short term. In general, however, longer follow-up periods are needed. Long follow-up periods may appear irrelevant to policy makers since they pertain to periods far away from the present, but the natural development of cancers as well as the measures to fight the diseases are often long processes which require decades of follow-up. The chosen method of evaluation must look beyond the needs of policymaking and determine the appropriate follow-up periods mainly on the basis of the properties of the cancer of interest.

Material and Methods

Since 1958 every physician, pathologist, and cytologist notifies the Swedish Cancer Registry of each new cancer diagnosis in Sweden. The non-reporting rate has been estimated at less than 2% (16). The present survival study was based on all cancer cases reported to the registry between 1961 and 1989. For all practical purposes this is a complete list of all the cancer cases during the study period. Excluded from the analysis were multiple tumors in the same anatomical site, autopsy findings, and patients who were 90 years or older at diagnosis. Some sites and some histopathological groups within sites were excluded from the analysis due to low incidence, and some histopathological groups within the same site were analyzed separately (e.g., seminomatous and non-seminomatous testis cancers). The registry does not include basalioma as part of the non-melanoma skin cancer group. On the other hand, all benign and malignant tumors of the endocrine glands are registered and were included in the analysis. A majority of these tumors were histologically benign, and the benign forms increased their share of the total number endocrine tumors over time.

A total of 388 393 men and 385 088 women with 37 different forms of cancer were included in the analysis. The cancer registry file was linked to all deaths reported to the national death registries up to and including December 31, 1991. Hence, all deaths except those occurring among the some 0.3% who were lost to follow-up before the termination date were recorded. This means that complete follow-up information was available for virtually all of the registered cases.

Consecutive cumulative crude survival proportions, CS_i , were computed for $i = \{1, 2, \dots, n\}$ years following diagnosis according to the life table method (17). The trends were analyzed using moving 3-year averages. Each computed CS curve pertained to three calendar years of diagnosis j to $j+2$ for $j = \{1961, 1962, \dots, 1987\}$. This yielded CS curves of length $n = 1992 - j + 2$ based on consecutively overlapping data. The first CS curve pertained to diagnoses in 1961-1963 and had a follow-up of 29 years, the second to cases diagnosed in 1962-1964 with 28 years of follow-up, etc. The last group diagnosed in 1987-1989 was followed for 3 years after diagnosis.

The cumulative relative survival rates RSR_i were computed as the ratio of the cumulative crude survival curve for the cancer group and the corresponding cumulative curve for the general population in the same calendar time period, $RSR_i = CS_{i,cancer} / CS_{i,population}$. The $CS_{i,population}$ curve was weighted by the observed age distribution in the cancer group at the time of diagnosis (18).

A decrease in RSR_i across years of follow-up is normally interpreted as continuing excess mortality in the cancer group over time. When the slope of the relative survival curve stabilizes at a horizontal level the cancer group has reached the same survival rate as the reference group from the 'normal' population.

The discontinued decrease of RSR_i is sometimes interpreted as an indication of cure on the individual level. However, if age matching is performed only at the beginning of follow-up, the cancer and population groups become increasingly dissimilar in terms of age composition over the years after diagnosis. The annual increase in average age is usually greater in the population than it is in the cancer group due to high mortality among elderly cancer patients. Hence, even after the survival curves of the population and cancer groups become parallel, a conditional survival disadvantage can be assumed to persist for individuals once diagnosed with cancer. It would be possible to account for this by using more stringent criteria for cure, e.g., by using a conditional RSR .

On the other hand, the determination of the cure rate usually requires very long follow-up periods. In the presence of an upward trend in RSR , cure rates based on very stringent criteria and applied to old data may exaggerate the present disadvantage of the cancer patients by not being able to take the recent improvements in diagnosis and treatment into account. Hence, for the present data the unconditional stabilization rates may provide a reasonable compromise between the conditional cure rates and the 5-year RSR 's.

Results

We first comment on the results for all sites combined for males and females separately. Subsequently we treat site- and age-specific survival for each sex.

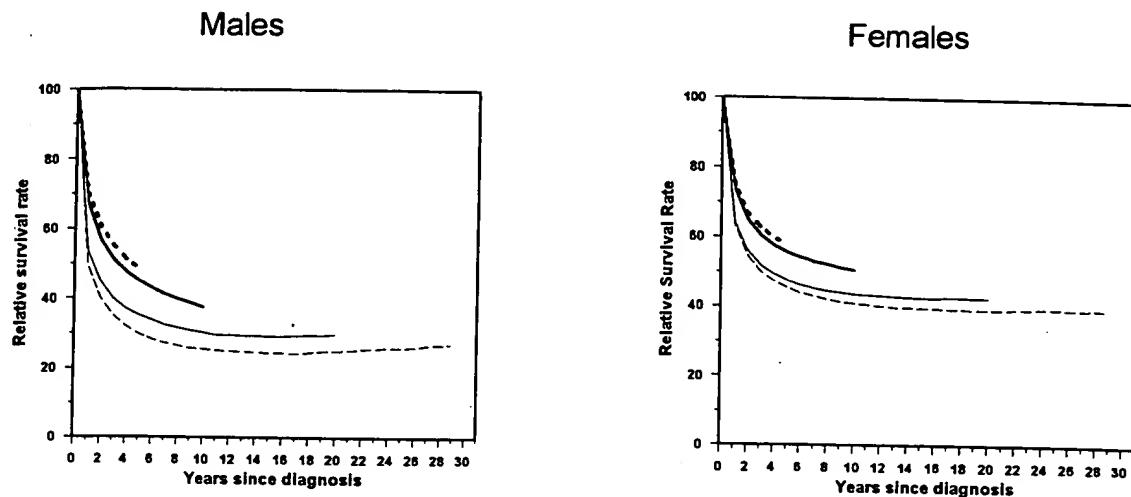


Fig. 1a. Relative survival for cancer patients diagnosed in 1961-1963 (-----), 1970-1972 (—), 1980-1982 (—), and 1985-1987 (....). All sites combined. Males and females 0-89 years of age at diagnosis.

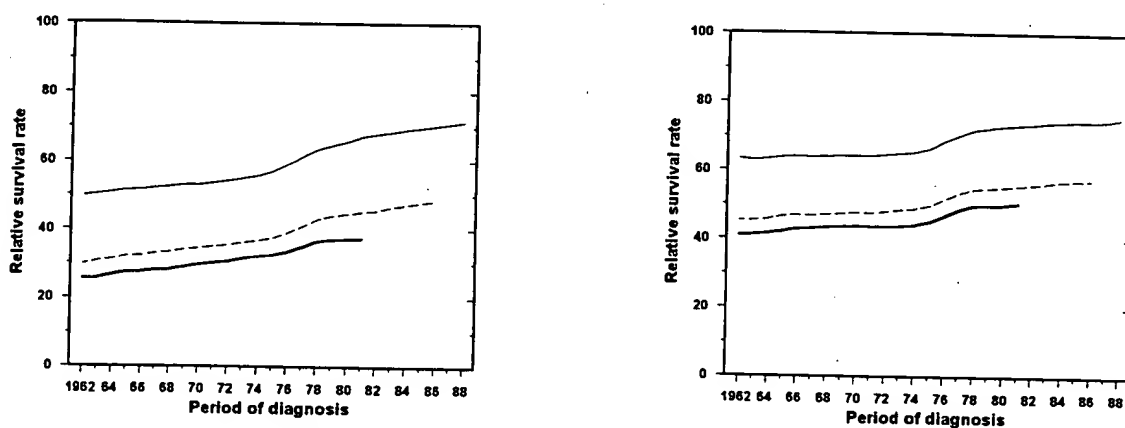


Fig. 1b. 1-year (—), 5-year (-----), and 10-year (—) relative survival rates of males and females 0-89 years of age diagnosis. 3-year moving averages.

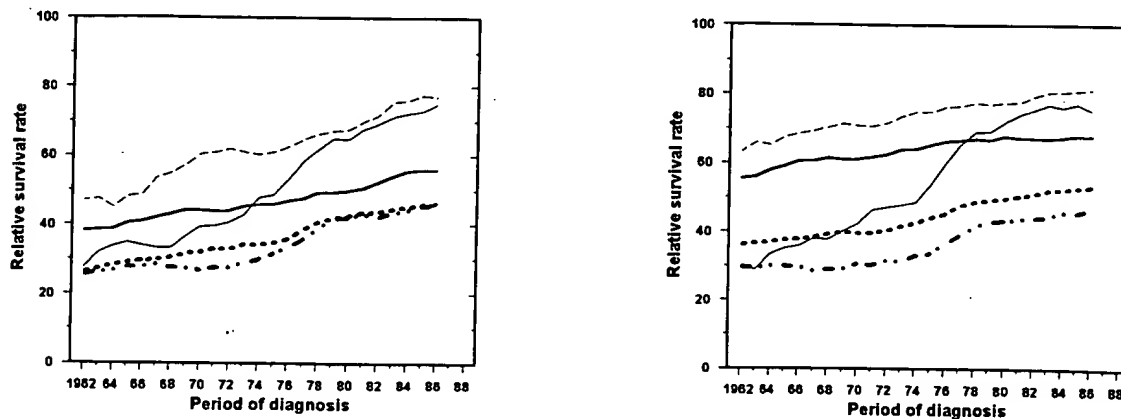


Fig. 1c. Age-group specific 5-year relative survival rates of males and females, 0-14 (—), 15-34 (-----), 35-54 (—), 55-64 (....), and 75-89 (- · -) years of age at diagnosis. 3-year moving averages.

Analysis of all sites

For all sites combined RSR increased in both sexes. The RSR curves decreased more slowly shortly after diagnosis for groups diagnosed in more recent periods (Fig. 1a). In addition, the curves took on a horizontal slope at higher levels. The time of stabilization was roughly the same for those who were diagnosed during the earlier and later periods. For patients diagnosed in 1970-1972 the stabilization occurred at 16 years for both sexes and at 29% for males and 43% for females.

Table 1 summarizes the development over time shown in Fig. 1b. The increases for 1-, 5-, and 10-year survival in each decade are expressed as percentage point differences. The comparison of the development in different decades is affected by the non-linearity of the percentage point scale, but in the present analysis the comparisons are justified by that the scale is approximately linear in the observed ranges.

The increases were slowest in the 1960's and fastest in the 1970's for both sexes (Table 1). The development during the 1980's was almost as slow as in the 1960's. For example, the annual percentage point increases of 5-year survival were twice as big during the 1970's as they were in the other two decades.

It is also evident that during the 1960's the development of mid- and long-term survival was faster than that of short-term survival (Table 1). This trend was reversed in the 1970's when short-term survival increased fastest and long-term survival slowest. In the 1980's, short- and mid-term survival seemed to develop at roughly the same pace for females, whereas the faster development of short-term survival persisted for males.

The 10-year RSR for males increased from 25% for cases diagnosed in 1961-1963 to 37% for the 1979-1981 group. The corresponding increase was from 41% to 50% for women. The main part of the increase took place in the 1970's.

Table 1

Relative survival rate (RSR). All sites. Level at beginning of decade (1961-1963, 1969-1971, 1979-1981) and average annual change in percentage points during decade

	1960's	1970's	1980's
Males			
1-year RSR	49.6 (0.4)	53.0 (1.3)	67.1 (0.7)
5-year RSR	29.8 (0.6)	34.5 (1.0)	44.5 (0.4)
10-year RSR	25.4 (0.5)	29.8 (0.7)	37.2 (no data)
Stabilization rate	24.6 (0.5)	29.1 (no data)	not available
Females			
1-year RSR	63.3 (0.1)	64.3 (0.9)	73.1 (0.3)
5-year RSR	45.3 (0.3)	47.5 (0.8)	55.2 (0.4)
10-year RSR	41.0 (0.4)	43.8 (0.6)	50.1 (no data)
Stabilization rate	39.3 (0.4)	42.6 (no data)	not available

Cancers with poor survival decreased and cancers with better survival increased their relative shares of the total incidence. Direct standardization shows that 10-20% of the increases in RSR could be attributed to changes in the distribution of incidence across sites. In addition, the age distribution of the incidence changed. Cancer became relatively more common in the age group 65-74 compared to the age groups 35-54 and 55-64 (Fig. 1c). Since older groups often have lower RSR than younger groups this change should have affected the slope of the RSR curve negatively. The impact of the shift in age distributions was small for all sites combined—only some 1-2% on the RSR trends. As shown below, the aging of the cancer population had greater effects for some specific sites. Most of the observed increases were nevertheless due to other factors than the redistributions of age and site.

Site-specific analysis

Some 80-90% of the increase in 'all sites' was due to site specific increases in RSR rather than increases in the incidence of less malignant cancer forms. Increases in short- as well as long-term RSR were seen in 28 out of 37 analyzed anatomical sites. A couple of sites with poor general survival did show some increases in 1-year survival (e.g., lung cancer), whereas improvements were absent for longer follow-up periods (Fig. 1b).

The most substantial increases in long-term RSR were found for acute leukemia, meningioma, Hodgkin's disease, malignant melanoma, and cancers of the testis and breast (Fig. 2). However, breast cancer did not reach a stabilization rate during the observation period.

The higher rates for women were partly due to better survival for the female specific cancer sites, in particular breast and cervix. The RSR of cervical cancer increased slightly between 1970-1972 and 1980-1982, whereas no increase or even a slight deterioration occurred during the rest of the 1980's.

For men there were increases in the short- and mid-term RSR's of prostate cancer, but with a tendency towards elimination of the increase for long-term survival.

Less pronounced increases in survival, mainly achieved in the 1970s, were found for cancers of the oesophagus, colon, rectum, kidney, thyroid gland, brain, and malignant melanoma, while no improvements were found for cancers of the oral cavity, lung, liver, biliary tract, pancreas or multiple myeloma. In contrast to the general tendency, stomach cancer showed no increase in survival in the 1970's but improved somewhat in the 1980's. Lundegårdh et al. (1) did not reveal any improvement in survival for patients with gastric cancer diagnosed 1960-1978, but in the present study we could see an increase in survival after that period.

Many groups of cancer patients had poorer survival than the normal population long after 5 years of follow-

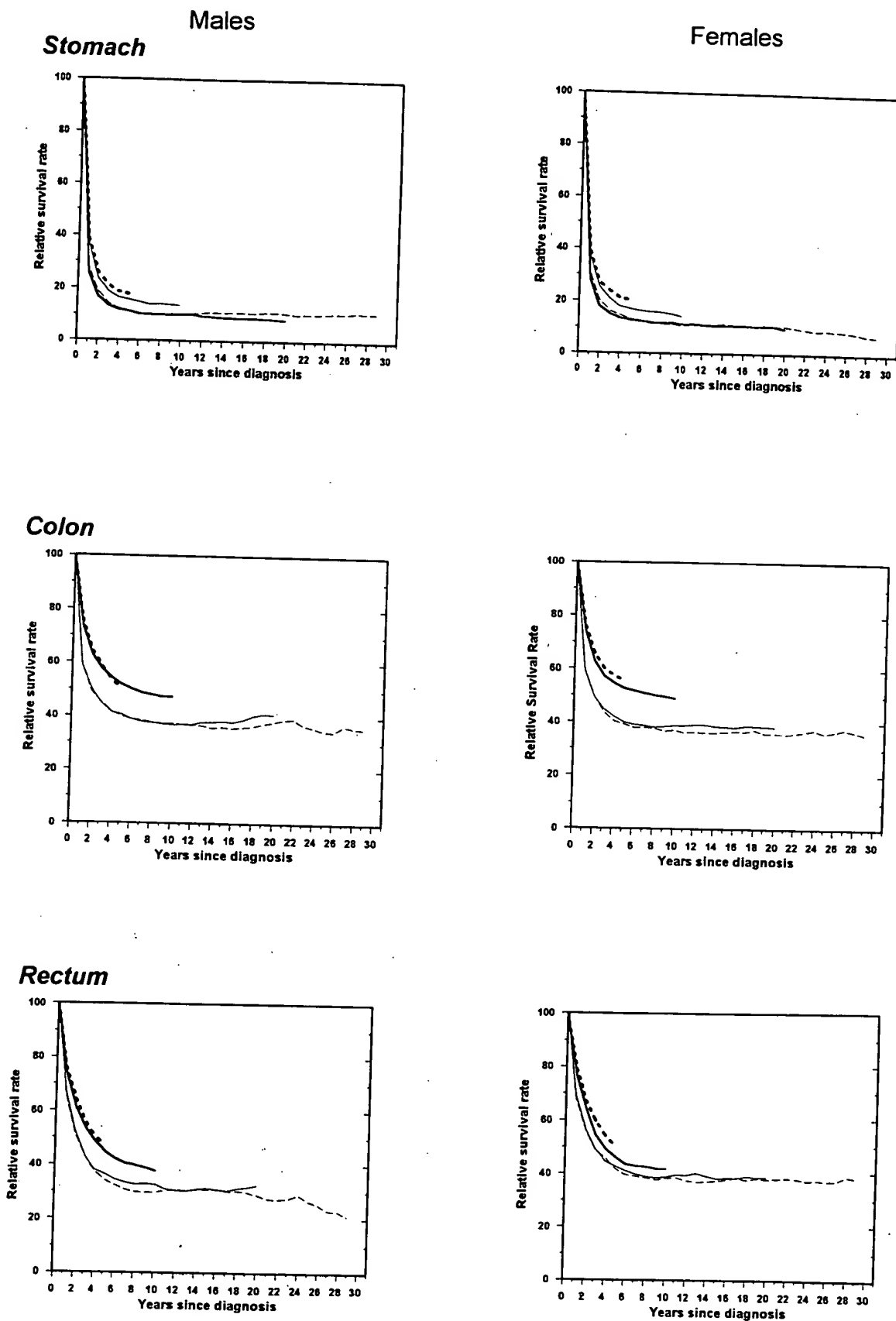


Fig. 2a. Relative survival for cancer patients diagnosed in 1961-63 (-----), 1970-1972 (—), 1980-1982 (——) and 1985-1987 (....). Males and females 0-89 years of age at diagnosis.

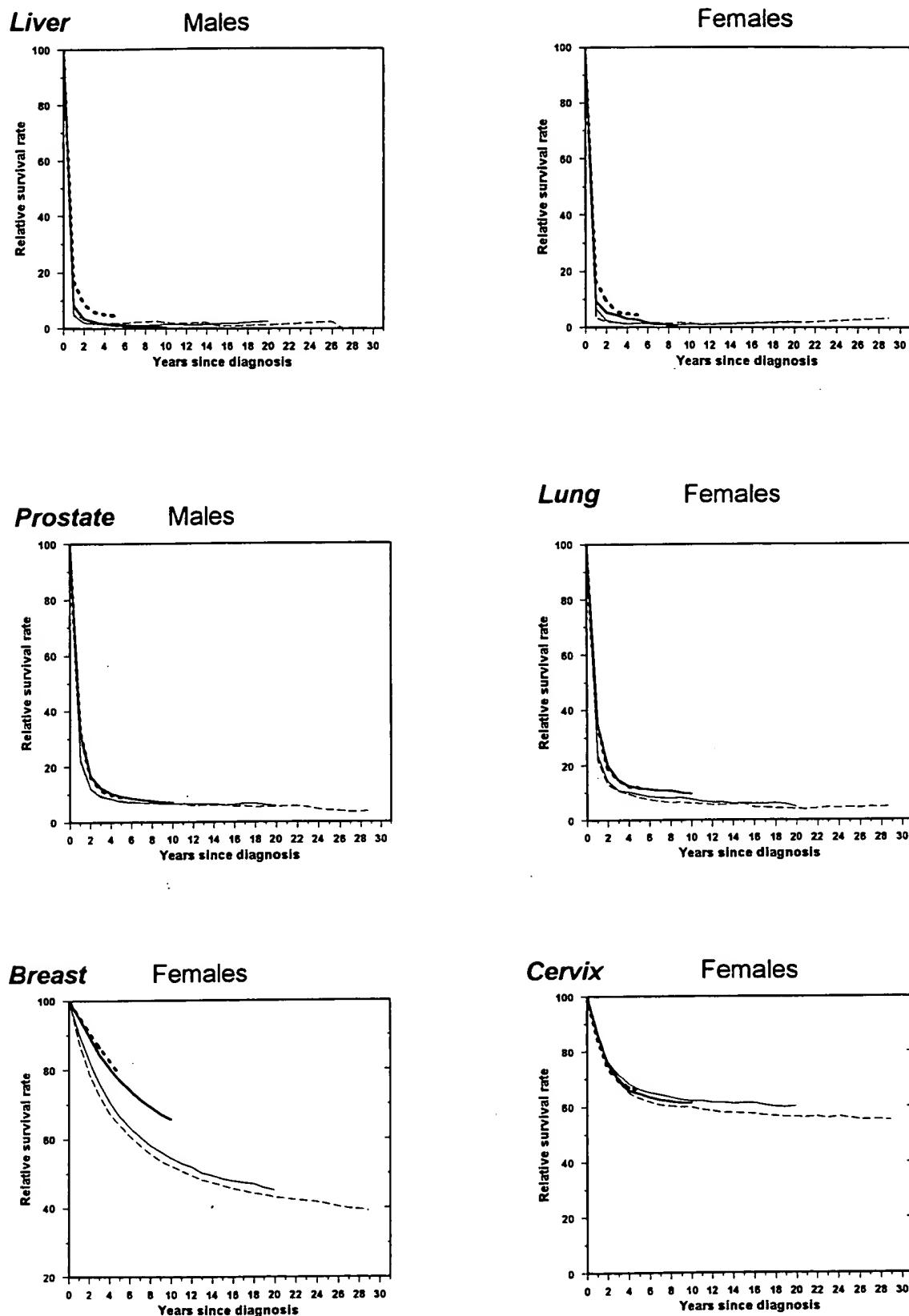


Fig. 2a. Relative survival for cancer patients diagnosed in 1961-63 (-----), 1970-1972 (—), 1980-1982 (——) and 1985-1987 (.....). Males and females 0-89 years of age at diagnosis.

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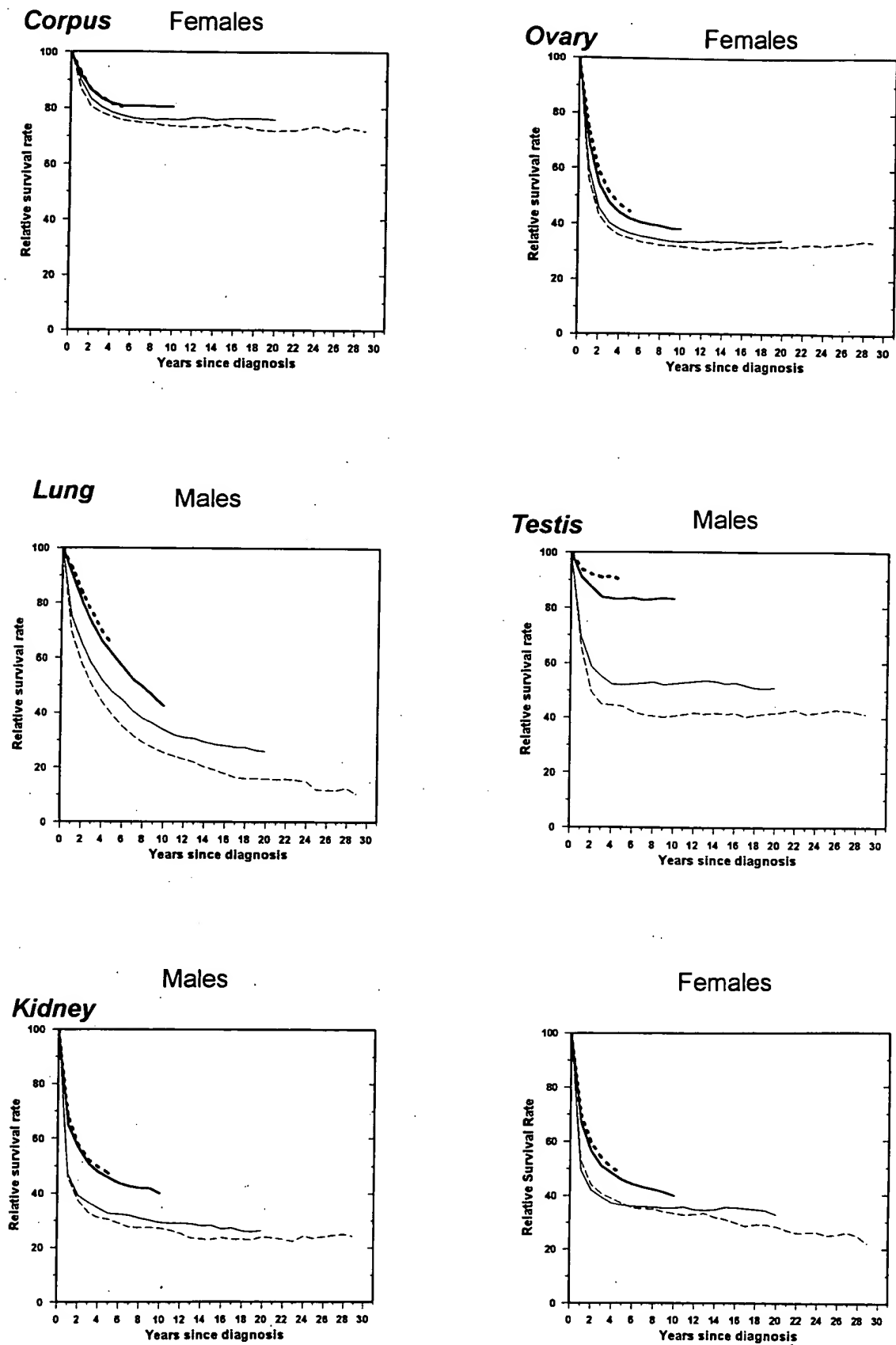


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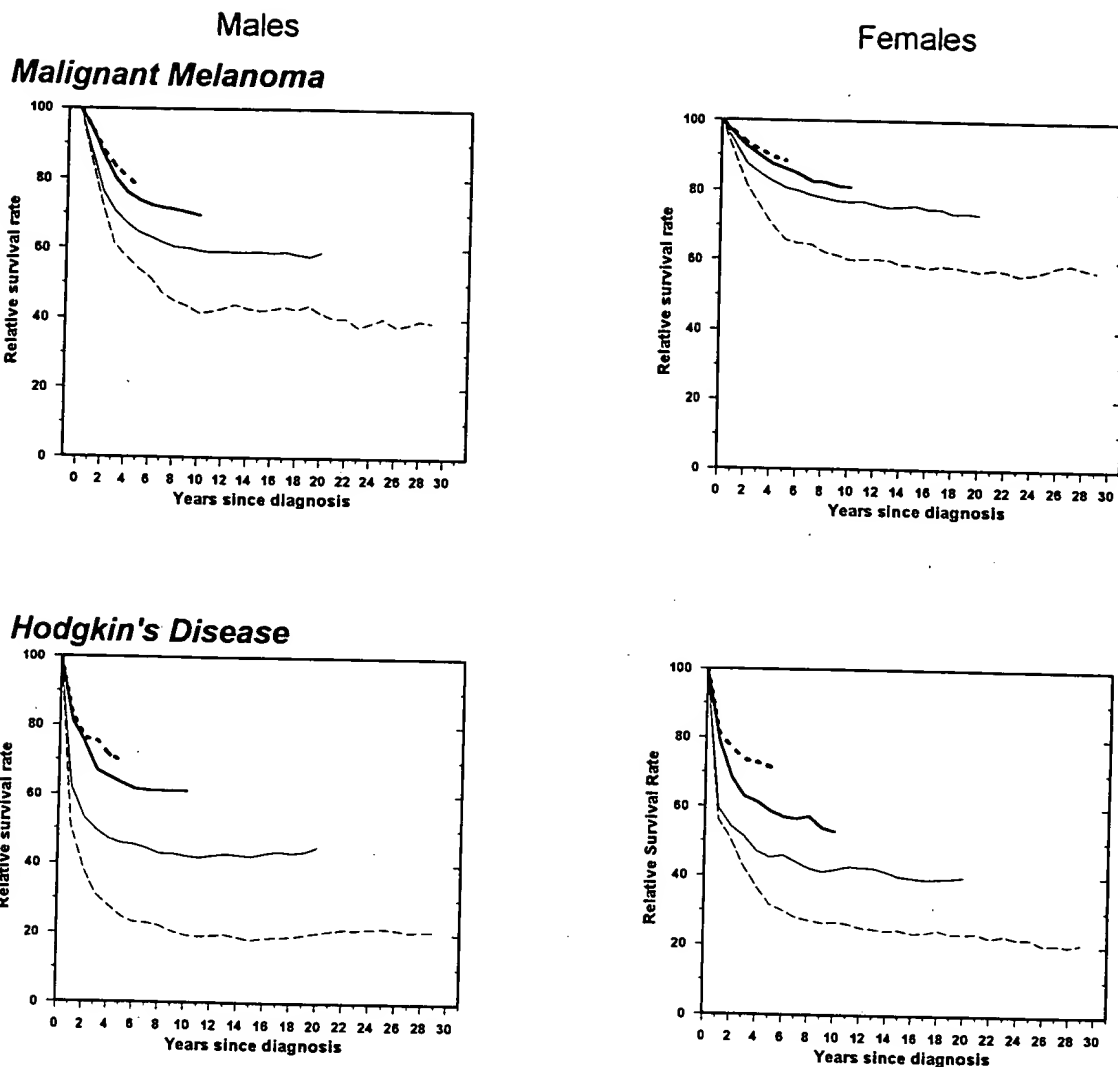


Fig. 2a. Relative survival for cancer patients diagnosed in 1961-63 (-----), 1970-1972 (—), 1980-1982 (—) and 1985-1987 (....). Males and females 0-89 years of age at diagnosis.

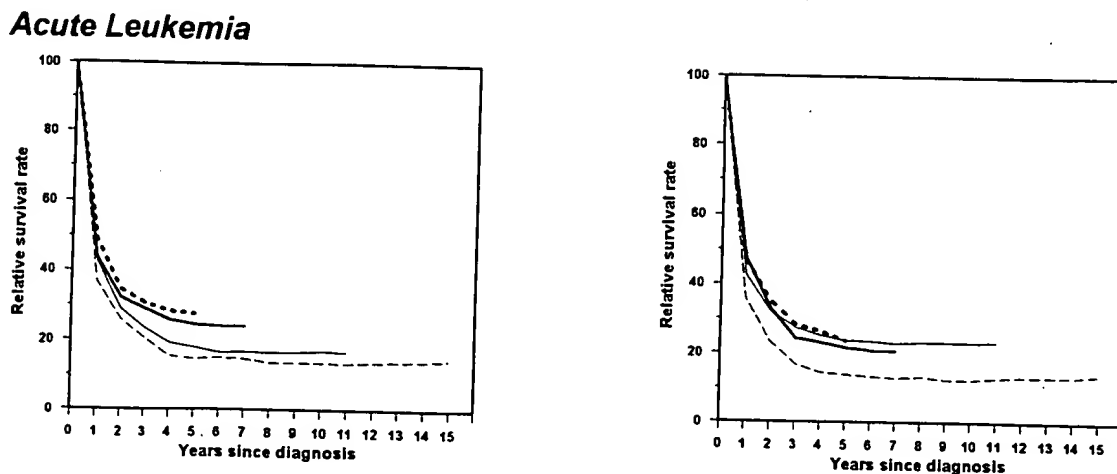


Fig. 2b. Relative survival for patients diagnosed with acute leukemia in 1975-77 (-----), 1979-1981 (—), 1983-1985 (—), and 1985-1987 (....). Males and females 0-89 years of age at diagnosis.

up. Female breast cancer patients had an excess risk of death even 20 years after diagnosis (6, 19), and the same was true for prostate cancer (20). In the present analysis the cancer patient groups diagnosed in 1970–1972 reached the survival patterns of the normal population of the same age at diagnosis after about 7–8 years for stomach cancer, 8–9 years for colon cancer, 8–12 years for rectum cancer, 10 years for cervical cancer, 7–10 years for malignant melanoma, 13–18 years for kidney cancer and more than 19 years for cancers of the female breast and prostate (Table 2).

The stabilization rates at those times were below 50% for many cancer sites. As mentioned earlier, for all sites combined cancer patients diagnosed in 1970–1972 reached the survival pattern of the reference group after 16 years at RSR's of 29% for males and 43% for females (Table 2). The stabilization rates for male cancer patients diagnosed in 1970–1972 varied from 0.6% for liver cancer to 88.8% for non-melanoma skin cancer. Similar variations were found for females.

Age-specific analysis

It was common that the younger age groups had better relative survival than the older groups throughout the

observed period ((9), Fig. 1c). This was true for leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, lung cancer, endometrial cancer, testis cancer, malignant melanoma, and meningioma.

For some sites the survival trend during the observed period differed between age-groups. A pronounced increase in survival was found for acute leukemia among persons under 55, whereas the development was not as positive for persons who were over 55 at diagnosis. The age-specific RSR's for cancer of the cervix showed a substantial increase for women 15–44 years of age while women 75–89 years of age had a negative development (9). In contrast, for the most common cancers, those of the female breast and prostate, we found greater progress in the older cohorts.

Discussion

The present study confirms earlier results in that substantial increases can be found for certain cancer sites, e.g., testis cancer, Hodgkin's disease, acute leukemia, cervical cancer among younger age cohorts and breast cancer (Fig. 2). A positive new finding is that the increased RSR in acute leukemia is not confined to children only. We found

Table 2

The level of RSR when the cancer group no longer has worse survival than the reference group and the years of follow-up until this occurs. Males and females diagnosed in 1970–1972. Selected sites

Cancer site	Approximate years of follow-up until stabilization		Unconditional 'stabilization rate'	
	Males	Females	Males	Females
Oral cavity	12	9	34.8	51.7
Stomach	8	8	10.3	11.3
Colon adenocarcinoma	8	9	37.5	39.5
Rectum adenocarcinoma	8	12	33.1	38.1
Liver	3	5	0.6	2.4
Pancreas	6	4	2.2	1.8
Lung	7	7	6.7	8.8
Breast	–	> 19	–	(46.3)
Cervix uteri	–	10	–	59.7
Corpus uteri	–	8	–	75.6
Ovary	–	12	–	32.9
Prostate	> 19	–	(24.5)	–
Testis seminoma	6	–	85.6	–
Kidney	18	13	27.4	33.1
Urinary bladder and urethra	7	9	60.4	62.3
Malignant melanoma	10	7	60.7	76.8
Skin cancer excl. melanoma	4	4	88.8	88.9
Hodgkin's disease	11	10	44.6	44.7
Non-Hodgkin's lymphoma	13	> 19	23.6	(23.1)
All sites	16	16	29.1	42.6

Note: The 'stabilization rate' is defined as the point estimate of the cumulative unconditional RSR at i when $RSR_{i+1} - RSR_i$ first is greater than or equal to zero. > 19 indicates that the RSR curve had not ceased to decrease at the end of follow-up (19 years). In those cases the estimate of RSR at 19 years of follow-up is given in parenthesis.

great increase in all age groups up to the age of 55. In light of other knowledge it may be concluded that improved treatment is a likely explanation for the substantial increases in RSR for testis cancer, acute leukemia, and Hodgkin's disease. These cancers represent less than 3% of the total cancer incidence in Sweden.

In contrast, increase of survival in female cancers may largely be attributed to early detection or to detection of biologically more benign tumors. Both these trends may be connected to the screening efforts introduced during the period even if the main effect of Pap smear screening will be noticed as a decrease in incidence since carcinoma *in situ* is not registered as an incidence case.

The increases in survival after diagnosis of intra-cranial neurinoma or cancers of the endocrine glands are probably mainly due to better postoperative survival in histologically benign tumor forms. This is suggested by the virtually perfectly horizontal appearance of the RSR curves after the first year since diagnosis for both early and late periods, but occurring at a much higher level for recent periods. The appearance of the RSR curves for meningioma suggest decreased postoperative mortality as a possible explanation as well. Enblad *et al.* (21) argued that improved survival of patients with colorectal cancer in Sweden during the 1960s and 1970s was due to reduced postoperative mortality. Our present study had a longer follow-up period for those diagnosed with colon cancer in the late 1970s. We were able to see increases in both short- and long-term RSR's during this time period, which suggests that reduced postoperative mortality is not the only reason for the increase.

For many cancer sites, *e.g.*, colorectal, ovarian, bone, and kidney cancer, there were only slight increases, mainly occurring in the 1970's. After the 1970's, we seem to be at a standstill. The reasons for the particularly positive increases in survival during the 1970's are not clear, but the marked increase in health care resources, decreased postoperative mortality, and the introduction of new diagnostic devices during this time period are some plausible explanations. Parts of the increased survival for some sites with increased diagnostic activity may be attributed to lead time bias, *i.e.*, early discovery not accompanied by real improvements in survival. Prostate cancer, and perhaps also non-Hodgkin's lymphoma, may be examples of this. Evidence from northern Sweden suggests that most of the improvements in prostate cancer survival disappear in stage-specific analyses (22).

Some cancers that did not show any progress had little potential for improvement due to already excellent survival records. In contrast, some others, such as cancers of the lung, liver, and pancreas, did not improve despite their very poor survival. For sites with this pattern and where the epidemiology is well known, actions to reduce incidence, such as decreased tobacco use, seems to be the only practicable way to fight the disease.

Adami *et al.* (8) stated that women's advantageous RSR for all sites combined could partly be due to the fact that female cancers, *e.g.*, breast cancer, have a more favourable prognosis compared with the survival rates for cancers dominated by males, *e.g.* lung cancer. A follow-up study suggested that the gender difference could be explained by female sex hormones preventing the establishment of distant metastases in certain malignant diseases (23). Wiebelt & Hakulinen (24) showed that the gender difference disappears when prognostic factors such as histology and tumor thickness are taken into account. The interpretation that women are more health conscious and seek medical care at an earlier stage is consistent with this. The present study shows that females had better RSR than men for many cancer sites which are not specific to or dominated by females, *e.g.*, oral cavity, malignant melanoma, thyroid gland, brain, colon, and rectum.

One of the most important results from the present study is that the main increase in RSR occurred during the 1970s and that the follow-up for those diagnosed in the late 1980s only showed marginal increases. A critical question is whether this indicates that we are at a standstill in the trend towards an improvement in cancer survival.

Policy implications

The policy implications of this overview are multifold. First, the fight against cancer is not lost. Substantial increases in long-term survival for cancer patients have been achieved. For some of the relatively rare cancer sites the increases were mainly due to better treatment, *e.g.*, leukemia for young patients, testis cancer, and Hodgkin's disease. For more common cancer sites with improved survival, *e.g.*, malignant melanoma, breast, and colorectal cancer, intensified diagnostic activity seems to have been the most important measure.

Second, the fight against cancer is far from won. Cancer patients still have much higher risks of dying than those of the same age and sex without cancer. The excess risk is apparent for many cancer sites even 8-10 years after the cancer has been diagnosed. For two of the most common cancer sites, prostate and breast cancer, there are excess death risks even after more than 20 years.

Third, reducing cancer incidence by primary prevention must still be the most promising and powerful intervention against cancer. The fact that cancer patients perceive much pain and suffering from the disease, and that no prolongation of life has occurred for many cancer forms, *e.g.*, cancers of the lung, liver, pancreas or oral cavity, speak in favour of a preventive strategy.

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REFERENCES

1. Lundegårdh G, Adami H-O, Malker B. Gastric cancer survival in Sweden. Lack of improvement in 19 years. *Ann Surg* 1986; 204: 546-51.
2. Graf W, Glimelius B, Pahlman L, Bergström R. Determinants of prognosis in advanced colorectal cancer. *Eur J Cancer* 1991; 27: 119-23.
3. Adami H-O, Malker B, Rutqvist L-E, Persson I, Ries L. Temporal trends in breast cancer survival in Sweden: significant improvement in 20 years. *JNCI* 1986; 76: 653-9.
4. Adami H-O, Glimelius B, Sparén P, Holmberg L, Krusemo UB, Pontén J. Trends in childhood and adolescent cancer survival in Sweden 1960 through 1984. *Acta Oncol* 1992; 31: 1-10.
5. Vågerö D, Persson G. Cancer survival and social class in Sweden. *J Epidemiol Community Health* 1987; 41: 204-9.
6. Rutqvist LE. On breast cancer incidence and survival. (Thesis) Stockholm: Department of General Oncology, Radiumhemmet, Karolinska Hospital, 1983.
7. Osterman B, Jonsson H, Tavelin B, Lenner P. Non-Hodgkin's lymphoma in northern Sweden: prognostic factors and response to treatment. *Acta Oncol* 1993; 32: 507-15.
8. Adami H-O, Sparén P, Bergström R, Holmberg L, Krusemo UB, Pontén J. Increasing survival trend after cancer diagnosis in Sweden: 1960-1984. *JNCI* 1989; 81: 1640-7.
9. Stenbeck, M, Rosén M, editors. Cancer survival in Sweden in 1961-1991. *Acta Oncol* 1995; 34 (Suppl 4).
10. Cancer Registry of Norway. Survival of cancer patients: cases diagnosed in Norway 1953-1967. Oslo: Norwegian Cancer Society, 1975.
11. Cancer Registry of Norway. Survival of cancer patients: cases diagnosed in Norway 1968-1975. Oslo: Norwegian Cancer Registry, 1980.
12. Hakulinen T, Pukkala E, Hakama M, Lehtonen M, Saxén E, Teppo L. Survival of cancer patients in Finland in 1953-1974. *Ann Clin Res* 1981; 13 (Suppl 31).
13. Carstensen B, Storm HH, Schou G, editors. Survival of Danish cancer patients 1943-1987. *APMIS* 1993; 101 (Suppl 33).
14. Berkson J, Gage RP. Survival curve for cancer patients following treatment. *J Am Stat Ass* 1952; 47: 501-15.
15. Easson EC, Russell MH. The curability of cancer in various sites. London: Pitman Medical Publishing Company Ltd, 1968.
16. Mattson B, Wallgren A. Completeness of the Swedish Cancer Register. Non-notified cancer cases on death certificates in 1978. *Acta Radiol Oncol* 1984; 23: 305-13.
17. Cutler SJ, Ederer F. Maximum utilization of the life table method in analyzing survival. *J Chron Dis* 1958; 8: 699-712.
18. Ederer F, Axtell LM, Cutler SJ. The relative survival rate: A statistical methodology. *NCI Monograph* No 6, 1961.
19. Brinkley D, Haybittle JL. The curability of breast cancer. *Lancet* 1975; 1: 95-7.
20. Aus G, Hugosson J, Norlén L. Long-term survival and mortality in prostate cancer treated with noncurative intention. *J Urol* (in press).
21. Enblad P, Adami H-O, Bergström R, Glimelius B, Krusemo UB, Pahlman L. Improved survival of patients with cancers of the colon and rectum? *JNCI* 1988; 80: 586-91.
22. Grönberg H, Bergh A, Damber J-E, Jonsson H, Lenner P, Ångström T. Prostate cancer in Northern Sweden. Incidence, survival and mortality in relation to tumour grade. *Acta Oncol* 1994; 33: 359-63.
23. Adami HO, Bergström R, Holmberg L, Klareskog L, Persson I, Pontén J. The effect of female sex hormones on cancer survival. A register-based study in patients younger than 20 years at diagnosis. *JAMA* 1990; 263: 2189-93.
24. Wiebelt H, Hakulinen T. Do women survive cancer more frequently than men? *JNCI* 1991; 83: 579.

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